U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

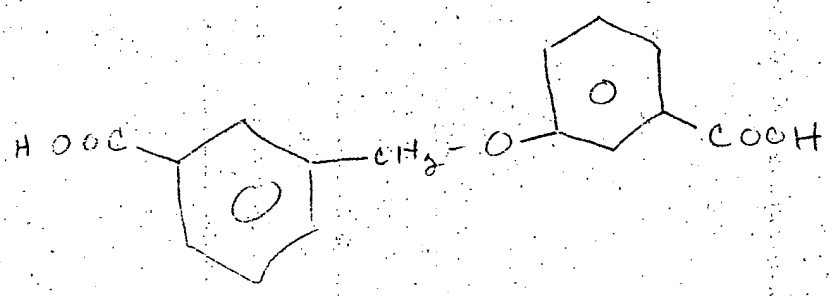
Requestor's Name: Spivack 70400 Serial Number: 09-995277

Date: 1-16-03 Phone: _____ Art Unit: 1614

2D05

9/11/98

Search Topic:
Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).



in Marpat

7.186

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

7 17
137

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=> fil marpat; d stat que l3
FILE 'MARPAT' ENTERED AT 08:37:20 ON 17 JAN 2003
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE CONTENT: 1988-PRESENT (VOL 104 ISS 15-VOL 138 ISS 2)(20030110/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US     6495149 17 DEC 2002
DE.   20211496 19 NOV 2002
EP     1264847 11 DEC 2002
JP  2002363748 18 DEC 2002
WO  2002099435 12 DEC 2002

Structure search limits have been raised.  See HELP SLIMIT for the new,
higher limits.
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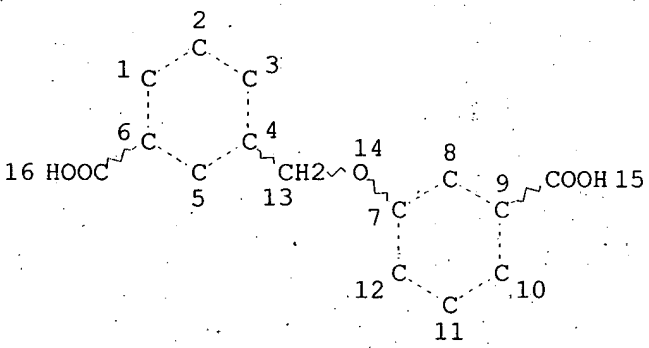
L1 STR

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NODE ATTRIBUTES:
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CONNECT IS E2  RC AT  10
CONNECT IS E2  RC AT  11
CONNECT IS E2  RC AT  12
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  1  2  3  4  5  6  7  8  9 10 11 12
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L2            57 SEA FILE=MARPAT SSS FUL L1
L3            55 SEA FILE=MARPAT ABB=ON  L2/COMPLETE

=> d ibib abs hit

L3   ANSWER 1 OF 55  MARPAT  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         137:346134  MARPAT
TITLE:                    Anti-infective agents and drug efflux pump inhibitors

                          Searched by Barb O'Bryen, STIC  308-4291
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Ex. Spivack,
As I mentioned, Marpat structures are difficult to read. My recommendation would be to look at the abstracts & dates. If you find a reference that looks promising, get a copy of the patent & evaluate the structures in it.
Barb

containing heteroaromatic compounds and

INVENTOR(S): Hoshino, Kazuki; Ishida, Hiroko; Omovskaya, Olga; Dudley, Michael; Rleger, Roger; Watkins, William John; Zhang, Jason Zhijia; Renau, Thomas Eric; Lee, Ving Jack; Ota, Toshiharu; Nakayama, Kiyoshi; Ishida, Yohei; Otsuka, Masami; Kawato, Haruko

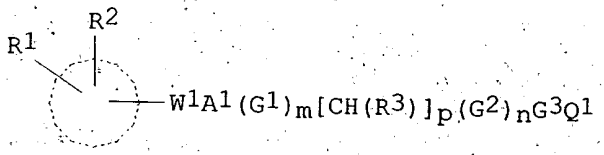
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan; Microcide Pharmaceuticals Inc.

SOURCE: Jpn. Kokai Tokkyo Koho, 95 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002322054	A2	20021108	JP 2001-130247	20010426

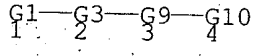
PRIORITY APPLN. INFO.: JP 2001-130247 20010426
GI



I

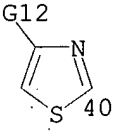
AB The pharmaceuticals, which are used for prevention and/or treatment of infections as mixts. with .gtoreq.1 antimicrobial agents, contain heteroarom. compds. I [R1, R2 = H, halo, CO2H, alkoxycarbonyl, (un)substituted amino, alkyl, aryl, heterocyclyl, R1 and R2 may be bonded together to form a 5-7-membered (un)satd. ring; R3 = H, OH, alkoxy; J1 = 5-6-membered heteroaryl; W1 = CH:CH, C.tplbond.C, CH2CH2, OCH2, SCH2, OCH2O, CH2O, CH2, CO, (CH2)3, CH2NH, NHCH2, CH2S, CONH, CH2SCH2, CH:CHCONH, CH2OCH2, direct bond; A1 = (un)substituted phenylene, heteroarylene such as pyridinediyl, furandiyl, benzo[b]thiophenediyl, benzoxazolediyl, quinolin-4-onediyl, thiazolo[3,2-a]pyrimidinediyl, etc.; G1 = O, CO, ethynyl, CH:N, NR4CO, CH2NR5CO, NR6, etc. (R4-R6 = H, OH, alkyl); p = 0-3; G2 = (un)substituted phenylene, heteroaryl such as furandiyl, pyridinediyl, thiazolidinediyl, etc.; G3 = CH2, direct bond; m, n = 0, 1; Q1 = acidic group], their physiol. acceptable salts, or their hydrates. The pharmaceuticals are esp. useful for treatment of infections with resistant bacteria. Cooperative effect of I, e.g. 2-[2-oxo-2-3-[(E)-2-(4-phenyl-1,3-thiazol-2-yl)-1-ethenyl]anilinoethyl]benzoic acid (prepn. given), with levofloxacin or aztreonam on Pseudomonas aeruginosa PAM1723 which highly expressing drug efflux pump was shown.

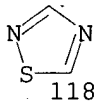
MSTR 1

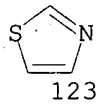


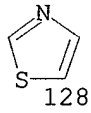
G1 = **heteroaryl<EC (3-10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (-2) G2)** / (EX 40 / pyridyl / 118 / 2-furyl / 123 / 128 / 132 / 2-thienyl)

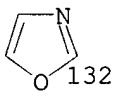
G12











G2 = F / Cl / Br / I / **CO2H** / alkoxycarbonyl<(1-8)> / cycloalkyloxycarbonyl<(3-8)> / NH2 (SO) / alkyl<(1-8)> (SO) / cycloalkyl<(3-8)> (SO) / aryl<(-14)> (SO) / Hy<EC (3-8) A> (SO)

G3 = phenylene (SO) / Hy<EC (5-10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO) / 9-1 10-3

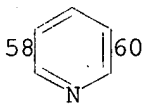
G4—G8
9 10

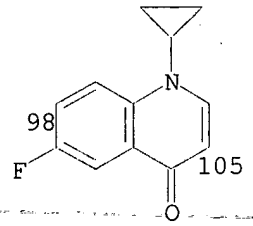
G4 = CH=CH / ethynylene / CH2CH2 / **11-1 12-10** / 13-1 15-10 / 17-1 18-10 / CH2 / C(O) / CH2CH2CH2 / 19-1 20-10 / 21-1 23-10 / 24-1 27-10

G5—CH2 (11 12) O—CH2—O (13 15) H2C—G6 (17 18) C(O)NH (19 20) H2C—G7—CH2 (21 23)

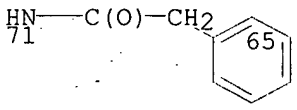
HC=CH—C(O)NH
24 27

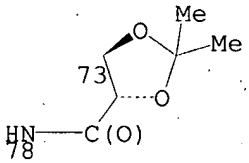
G5 = **O** / S / NH
G6 = O / NH / S
G7 = O / S
G8 = **phenylene (SO)** / Hy<EC (5-10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO) / (EX 58-9 60-3 / 98-9 105-3)

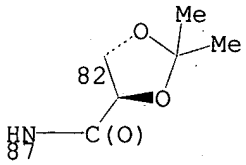


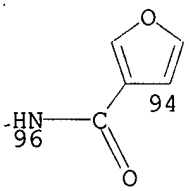


G9 = NULL / R<TX "linking group"> / (EX 71-2 65-4 / 78-2 73-4 / 87-2 82-4 / 96-2 94-4)



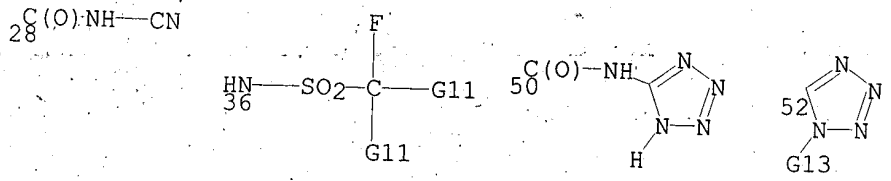






G10 = R<TX "acidic group"> / **(EX CO2H** / 28 / 36 / alkoxycarbonyl<(1-8)> (SO) / cycloalkyloxycarbonyl<(3-8)>

(SO) / 50 / 52)



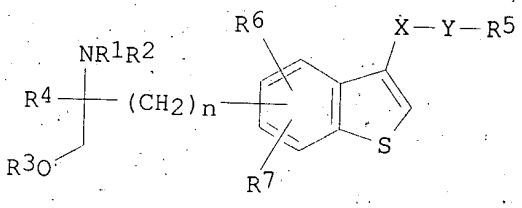
G11 = H / F
G12 = Ph / Pr-i
G13 = H / R
MPL: claim 1
NTE: or physiologically acceptable salts and hydrates
NTE: additional ring formation also claimed

=> d ibib abs hit 2-55; fil hom

L3 ANSWER 2 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:337773 MARPAT
TITLE: Immunosuppressant benzothiophene derivatives
INVENTOR(S): Nishi, Takehide; Shiroshima, Takaaki; Shimozato, Ryuichi; Nara, Futoshi
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 67 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002316985	A2	20021031	JP 2001-122867	20010420

PRIORITY APPLN. INFO.: JP 2001-122867 20010420
GI

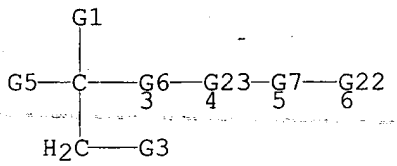


I

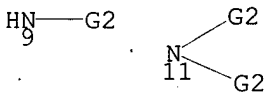
AB The derivs. I [R1, R2 = H, amino-protecting group; R3 = H, hydroxy-protecting group; R4 = lower alkyl; n = 1-6; X = CH2CH2, CH:CH, C.tplbond.C, DCH2 (D = CO, CHOH, O, S, N), aryl which may be substituted with .gtoreq.1 selected from (a) (definition given); Y = direct bond, C1-10 alkylene which may be substituted with .gtoreq.1 selected from (a) and (b) (definition given) and/or contain O or S in the chain; R5 = H, cycloalkyl, aryl, heterocyclyl, which may be substituted with .gtoreq.1 selected from (a) and (b); R6, R7 = H, any group selected from (a); if R5 = H, then Y = any group other than direct bond, n-C1-10 alkylene], their pharmacol. acceptable salts, their esters, and their derivs. show low

cytotoxicity and are useful as immunosuppressants. Prepn. of (2R)-amino-4-[3-(4-cyclohexyloxybut-1-ynyl)benzo[b]thiophen-6-yl]-2-methylbutan-1-ol was given. I showed high suppressive activity on host vs. graft reaction in rats.

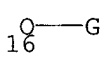
MSTR 1



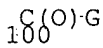
G1 = NH2 / 9 / 11



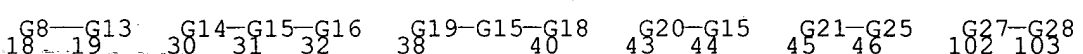
G2 = R<TX "protecting group"> /
(SC alkoxycarbonyl<(1-6)> / alkoxycarbonyl (SR (1-) G26))
G3 = OH / 16

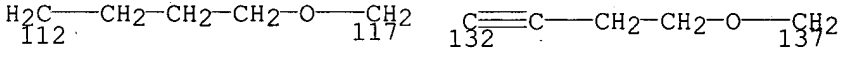


G4 = R<TX "protecting group"> / (SC 100 /
arylcarbonyl<(6-10)> (SO (1-3) G9))

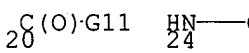


G5 = alkyl<(1-6)> / (SC Me / Et)
G6 = (1-6) CH2
G7 = 18-4 19-6 / arylene<(6-10)> (SO (1-3) G9) /
Ak<EC (2-12) C, BD (-1) D (-1) T> (SO (1-3) G12) /
30-4 32-6 / 38-4 40-6 / 43-4 44-6 / 45-4 46-6 /
(SC 102-4 103-6 / 112-4 117-6 / 132-4 137-6)

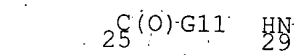




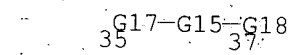
G8 = C(O) / CHOH / O / S / NH
G9 = F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G10) /
alkoxy<(1-6)> / alkylthio<(1-6)> / **CO2H** /
alkoxycarbonyl<(1-6)> / OH / 20 / NH2 / alkylamino<(1-6)> /
dialkylamino<(1-6)> / 24 / CN / NO2



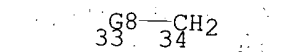
G10 = F / Cl / Br / I
G11 = H / Ak<(1-6)>
G12 = F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G10) / alkoxy<(1-6)> / alkylthio<(1-6)> / **CO2H** / alkoxycarbonyl<(1-6)> / OH / 25 / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / 29 / CN / NO2 / cycloalkyl<(3-10)> (SO) / aryl<(6-10)> (SO) / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RS (0-) E5 (0-) E6 (0-) E7 (0) OTHER> (SO)



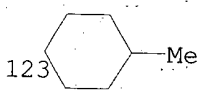
G13 = alkylene<(1-11)> (SO (1-3) G12) / 35-18 37-6 / 41-18 42-6

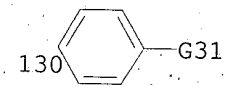


G14 = CH2CH2 / CH=CH / ethynylene / 33-4 34-31 / arylene<(6-10)> (SO (1-3) G9)

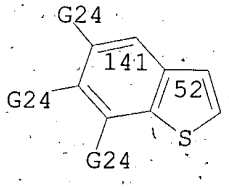


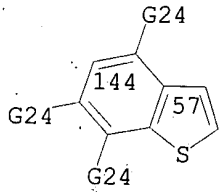
G15 = O / S
G16 = alkylene<(1-10)> (SO (1-3) G12)
G17 = alkylene<(2-10)> (SO (1-3) G12)
G18 = alkylene<(1-9)> (SO (1-3) G12)
G19 = Ak<EC (3-11) C, BD (-1) D (-1) T> (SO (1-) G12) / arylene<(6-10)> (SO (1-3) G12)
G20 = Ak<EC (3-11) C, BD (-1) D (-1) T> (SO (1-) G12)
G21 = arylene<(6-10)> (SO (1-3) G9)
G22 = H / cycloalkyl<(3-10)> (SO (1-3) G12) / **aryl<(6-10)> (SO (1-3) G12)** / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RS (0-) E5 (0-) E6 (0-) E7 (0) OTHER> (SO (1-3) G12) / (SC cyclohexyl / Ph (SO (1-3) G30) / 123 / 130)

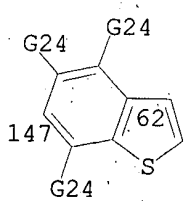


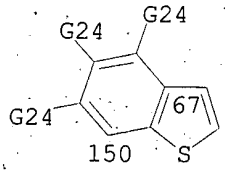


G23 = 141-3 52-5 / 144-3 57-5 / 147-3 62-5 / 150-3 67-5









G24 = H / F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G10) / alkoxy<(1-6)> / alkylthio<(1-6)> / CO2H / alkoxycarbonyl<(1-6)> / OH / 90 / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / 99 / CN / NO2

C(O)-G11 HN---C(O)-G11
90 99

G25 = alkylene<(1-10)> (SO (1-) G12) / 92-45 94-6 /
95-45 96-6

G18-G15-G18 G16-G15
92 94 95 96

G26 = aryl (SO (1-3) G9)
G27 = CH2CH2 / CH=CH / ethynylene / 104-4 105-103 /
arylene<(6-10)> (SO (1-3) G9)

G8---CH2
104 105

G28 = CH2CH2 / CH2CH2CH2 / CH2CH2CH2CH2 / **106-102 107-6** /
109-102 108-6

O---G29 G29-O
106 107 109 108

G29 = **(1-3) CH2**
G30 = F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G10) /
alkoxy<(1-6)> / 110 / Me / CF3 / OMe / COMe

C(O)-G11
110

G31 = Et / SMe
MPL: claim 1
NTE: or pharmacologically acceptable salts or esters
NTE: additional heteroatom interruptions also claimed
NTE: substitution is restricted

L3 ANSWER 3 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:196991 MARPAT
TITLE: Stable preservative formulations comprising antimicrobial halopropynyl compounds and butoxydiglycol solvent
INVENTOR(S): Borokhov, Olga; Lutz, Patrick Jay; Maroski, John G.
PATENT ASSIGNEE(S): Lonza Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002067685	A1	20020906	WO 2002-US6193	20020226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO,

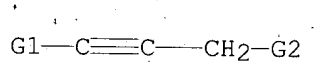
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-271760P 20010226

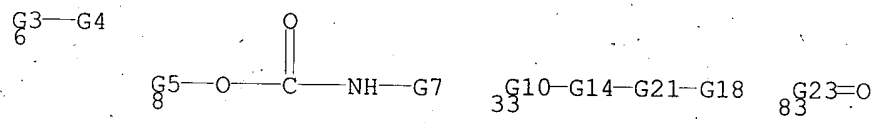
AB Liq. broad spectrum preservative formulations comprise (a) an antimicrobial halopropynyl compd, such as YC.tplbond.CCH2X (Y = halo, X = org. group contg. O,N,S, or C)and (b) a butoxydiglycol solvent, and, optionally, (c)(i) an alkanol substituted dialkylhdantoin formaldehyde donor, (ii) an antimicrobial isothiazolone deriv., and (iii) a stabilizer. The invention is also directed to methods of use of the preservative formulations for inhibiting or retarding the growth of bacteria or fungi.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

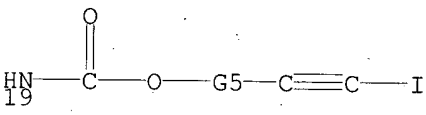
MSTR 1



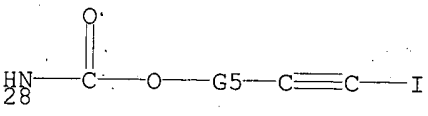
G1 = X / (SC I)
G2 = R<TX "organic group", EC (0-) N (0-) O (0-) S (0-) C> / (SC OH (SO) / CO2H (SO) / OCHO (SO) / OCONH2 (SO) / NH2 (SO) / CONH2 (SO) / 6 / 8 / 33 / Ak<BD (0-) D (0) T> (SO (1-) G19) / 83)



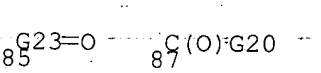
G3 = NH (SO)
G4 = CHO (SO)
G5 = alkylene<EC (1-3) C, DC (0) M3> (SO (1-) G6)
G6 = alkyl<(1-20)> (SO) / aryl<(6-20)> (SO) / alkyl<(1-14)> (SR (1-) aryl<(6-19)>)
G7 = alkyl<(1-20)> (SO (1-) G8) / aryl<(6-20)> (SO (1-) G8) / alkyl<(1-14)> (SR (1-) G9)
G8 = R / 19



G9 = aryl<(6-19)> (SO (1-) G8) / R / 28



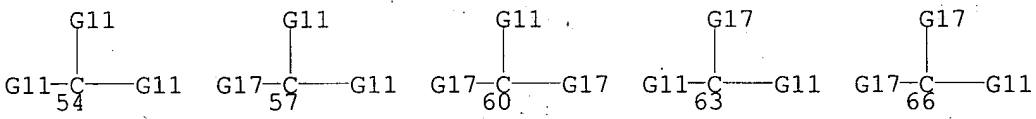
G10 = NULL / alkylene<EC (1-16) C, DC (0) M3> (SO (1-) G6)
G11 = Ak<BD (0-) D (0) T> (SO (1-) G19) / 85 / 87

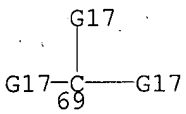


G12 = alkyl / cycloalkyl<(3-12)> / alkenyl / cycloalkenyl<(3-12)> / aryl<(6-15)> / alkoxy / NH2 / **CO2H** / X / OH / COSH
G13 = Hy<EC (5-15) A (0-) N (0-) O (0-) S> (SO (1-) G12)
G14 = 43 / cycloalkylene<(3-12)> (SO (1-) G15) / **cycloalkenylene<(3-12)> (SO (1-) G15)** / arylene<(6-15)> (SO (1-) G15) / Hy<EC (5-15) A (0-) N (0-) O (0-) S> (SO (1-) G15) / 45 / 48 / 51

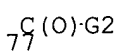
G15 = alkoxy / NH2 / **CO2H** / X / OH / COSH
G16 = Cb<(3-15)> (SO (1-) G15) / Hy<EC (5-15) A (0-) N (0-) O (0-) S> (SO (1-) G15)
G17 = H / cycloalkyl<(3-12)> (SO (1-) G12) / **cycloalkenyl<(3-12)> (SO (1-) G12)** / aryl<(6-15)> (SO (1-) G12) / Hy<EC (5-15) A (0-) N (0-) O (0-) S> (SO (1-) G12) / 40 / alkoxy / NH2 / X / OH

G18 = 54 / 57 / **60** / 63 / 66 / 69

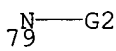




G19 = cycloalkyl<(3-12)> / cycloalkenyl<(3-12)> / aryl<(6-15)> / alkoxy / NH2 / 77 / X / OH



G20 = OH / SH
G21 = **O** / NH / 79



G22 = cycloalkyl<(3-12)> (SO (1-) G12) / cycloalkenyl<(3-12)> (SO (1-) G12) / aryl<(6-15)> (SO (1-) G12) / Hy<EC (5-15) A (0-) N (0-) O (0-) S> (SO (1-) G12) / 81 / Ak<BD (0-) D (0) T> (SO (1-) G19)

G13=O
81

G23 = Ak<BD (0-) D (0) T> (SO (1-) G19)
MPL: claim 2

L3 ANSWER 4 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:93763 MARPAT
TITLE: Preparation of chiral pyrrolidine derivatives as VLA-4 inhibitors
INVENTOR(S): Nakayama, Atsushi; Machinaga, Nobuo; Yoneda, Yoshiyuki; Sugimoto, Yuichi; Chiba, Jun; Watanabe, Toshiyuki; Iimura, Shin
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 737 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053534	A1	20020711	WO 2001-JP11641	20011228
WO 2002053534	C1	20020919		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-402890 20001228
JP 2001-149923 20010518

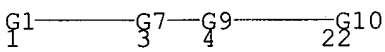
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

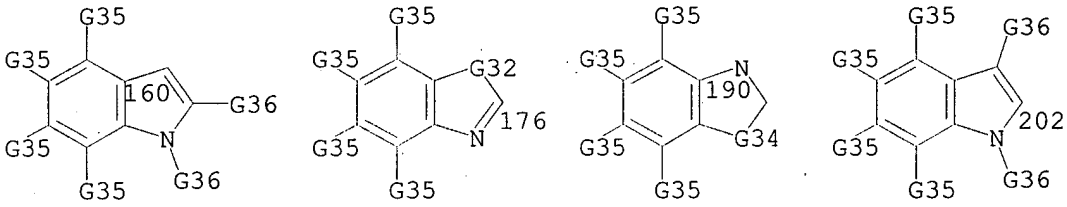
AB Title compds. [WRXM; W = WAA1WB; WA = optionally substituted aryl; A1 = NR1, single bond, C(O); WB = is optionally substituted arylene; R = single bond, NH, OCH2, alkenylene; X = C(O), CH2; M = group represented by the general formula I; R11, R12, R13 each independently = hydrogen, hydroxyl, amino, halogeno; R14 = hydrogen, alkyl; Y = CH2O; Z = optionally substituted arylene; A2 = single bond; R10 = hydroxyl, alkoxy; Q = CH2, S, O, NH], salts thereof, and medicines contg. the same are prepd. as VLA-4 inhibitors. Title compds. or salts selectively inhibit the binding of cell adhesion mols. to VLA-4 and exhibit high oral absorbability, thus being useful as preventive and/or therapeutic drugs for inflammatory diseases, autoimmune diseases, cancerous metastasis, bronchial asthma, nasal occlusion, diabetes, inflammatory enteric disease, arthritis, etc. The Title compd. II was prepd. from Et 4-amino-3-chlorophenylacetate, indoline, and Me [(4S)-fluoro-(2S)-pyrrolidinylmethoxy]cyclohexylcarbonate and the title compd. III was prepd. from Me 3-hydroxy-4-nitrophenylacetate, Ph isothiocyanate, and Me 4-[(4S)-fluoro-(2S)-pyrrolidinylmethoxy]benzoate.

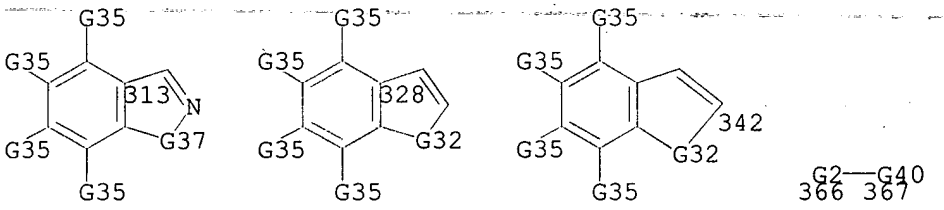
REFERENCE COUNT: 143 THERE ARE 143 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1

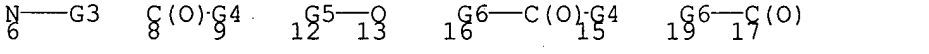


G1 = aryl<(6-18)> (SO) / Hy<EC (5-18) A (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-)> (SO) / 366 / (SC 160 / 176 / 190 / 202 / 222 / 237 / 253 / 270 / 285 / 300 / 313 / 328 / 342)



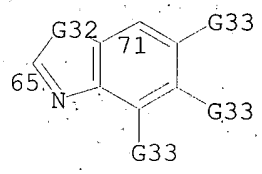


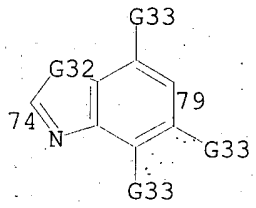
G2 = NH / 6 / C(O) / 8-367 9-3 / CH=CH (SO) / ethynylene / 12-367 13-3 / 16-367 15-3 / 19-367 17-3

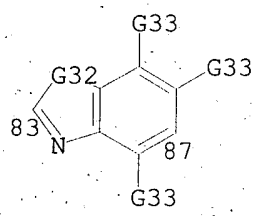


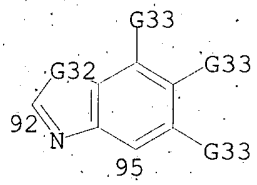
G3 = alkyl<(1-8)>
G4 = NH / 10

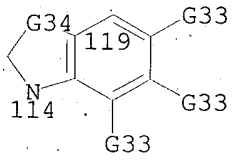
G5 = alkylene<(1-)>
G6 = alkenylene<(2-)>
G7 = arylene<(6-18)> (SO) /
Hy<EC (5-18) A (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-)> /
(SC 65-1 71-4 / 74-1 79-4 / 83-1 87-4 / 92-1 95-4 /
114-1 119-4 / 123-1 127-4 / 132-1 135-4 / 141-1 143-4)

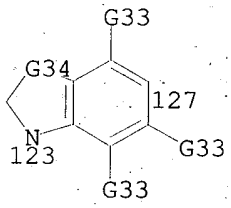


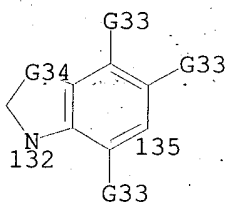


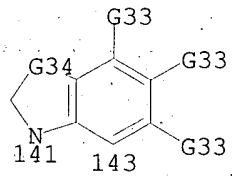




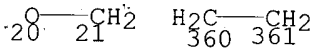




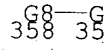




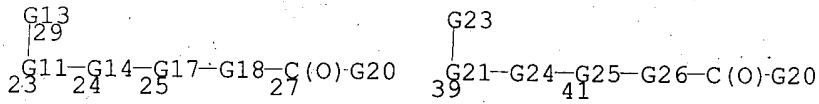
G8 = NH / 20-3 21-359 / alkenylene<(2-12)> / CH2 /
360-3 361-359

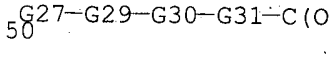


G9 = C(O) / CH2 / SO2 / 358-3 359-22



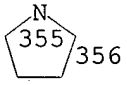
G10 = **23** / 39 / 50



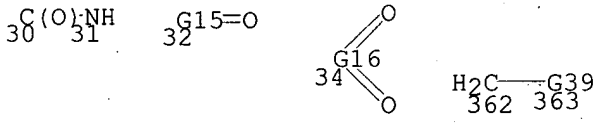


G11 = **Hy<EC (4-7) A (1-) N (0-) O (0-) S (0) OTHERQ,
AN (1-) N (1-) C, RC (1), RS (0-) E4 (0-) E5 (0-) E6 (0-)
E7 (0) OTHER> (SO (1-3) G12)** / Hy<EC (5-12) A (1-) N (0-)
O (0-) S (0) OTHERQ, RC (2), RS (0-) E3 (0-) E4 (0-) E5 (0-)

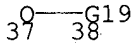
E6 (0-) E7 (0) OTHER> (SO (-1) G12) /
(SC 356-29 355-4 356-24)



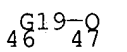
G12 = OH / NH2 / F / Cl / Br / I / CN / **CO2H** /
alkoxycarbonyl / CONH2 / alkylaminocarbonyl /
dialkylaminocarbonyl / alkyl<(1-12)> (SO) /
aryl<(6-18)> (SO) / heteroaryl<EC (5-18) A (0-) N (0-) O (0-)
S (0) OTHERQ, RC (1-)> (SO) / alkoxy (SO) / alkylamino (SO) /
dialkylamino (SO) / cycloalkylamino<(3-10)> (SO) /
alkylsulfonylamino (SO) / arylsulfonylamino (SO) /
aryloxy (SO) / heteroaryloxy<EC (5-18) A (0-) N (0-) O (0-)
S (0) OTHERQ, RC (1-)> (SO) / OCH2Ph (SO) / alkylthio (SO) /
cycloalkylthio (SO) / arylthio (SO) / alkylsulfonyl (SO) /
cycloalkylsulfonyl (SO) / arylsulfonyl (SO)
G13 = H / alkyl<(1-8)> (SO)
G14 = NULL / C(O) / 30-23 31-25 / Ak<(1-12)> / 32 / 34 /
(SC 362-23 363-25 / CH=CH / ethynylene)



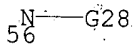
G15 = Ak<(1-12)>
G16 = R<TX "aliphatic chain containing sulfur atom">
G17 = **arylene<(6-18)> (SO)** /
heteroarylene<EC (5-18) A (0-) N (0-) O (0-) S (0) OTHERQ,
RC (1-)> (SO) / cycloalkylene<(3-10)> (SO)
G18 = NULL / alkenylene<(2-12)> /
alkynylene<EC (2-12) C, BD (1) T> / G19 / O / 37-25 38-27



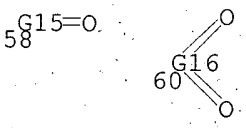
G19 = (1-3) CH2
G20 = **OH** / alkoxy<(1-8)>
G21 = Hy<EC (4-7) A (1-) N (0-) O (0-) S (0) OTHERQ,
AN (1-) N (1-) C, RC (1), RS (0-) E4 (0-) E5 (0-) E6 (0-)
E7 (0) OTHER> (SO (1-2) G22)
G22 = OH / F / Cl / Br / I / alkyl<(1-12)> (SO) /
alkoxy (SO)
G23 = H / alkyl<(1-12)> (SO)
G24 = O / S / SO2 / 46-39 47-41 / NH / 48



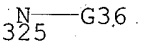
G25 = arylene<(6-18)> (SO) /
heteroarylene<EC (5-18) A (0-) N (0-) O (0-) S (0) OTHERQ,
RC (1-)> (SO) / cycloalkylene<(3-10)> (SO)
G26 = NULL / alkenylene<(2-12)> (SO) /
alkynylene<EC (2-12) C, BD (1) T> / G19
G27 = NH / 56



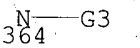
G28 = alkyl<(1-12)> (SO) / cycloalkyl<(3-10)> (SO) / aryl<(6-18)> (SO) / CH2Ph (SO) / alkenyl<(2-8)> (SO) / alkynyl<EC (2-12) C, BD (1) T>
G29 = Ak<(1-12)> / 58 / 60



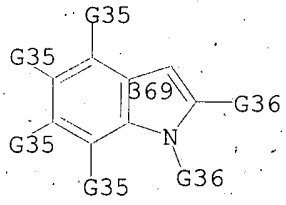
G30 = NULL / arylene<(6-18)> (SO) / heteroarylene<EC (5-18) A (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-)> (SO) / cycloalkylene<(3-10)> (SO)
G31 = NULL / alkylene<(1-8)> (SO) / alkenylene<(2-8)> (SO)
G32 = O / S
G33 = H / F / Cl / Br / I / alkyl<(1-8)> / OH / alkoxy<(1-8)> / NH2
G34 = (1-2) CH2
G35 = H / F / Cl / Br / I / alkyl<(1-8)> / OH / alkoxy<(1-8)> / NH2
G36 = H / alkyl<(1-8)>
G37 = O / S / 325

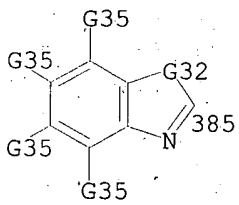


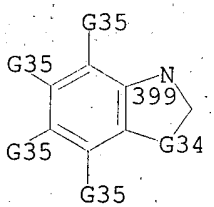
G38 = C(O) / CH2 / SO2
G39 = O / S / SO2 / CH2 / NH / 364

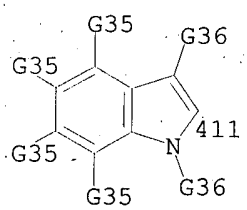


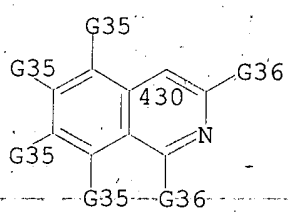
G40 = aryl<(6-18)> (SO) / Hy<EC (5-18) A (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-)> (SO) / (SC 369 / 385 / 399 / 411 / 430 / 447 / 465 / 478 / 495 / 512 / 521 / 534 / 548)

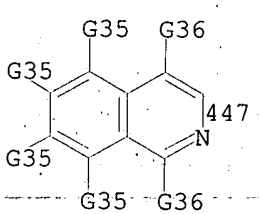


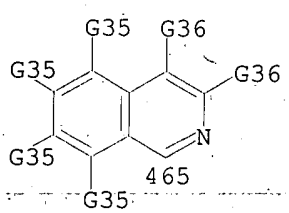


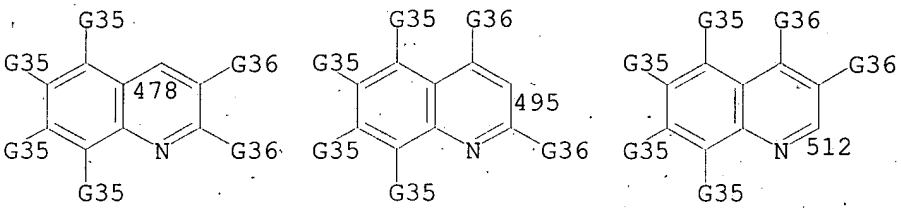


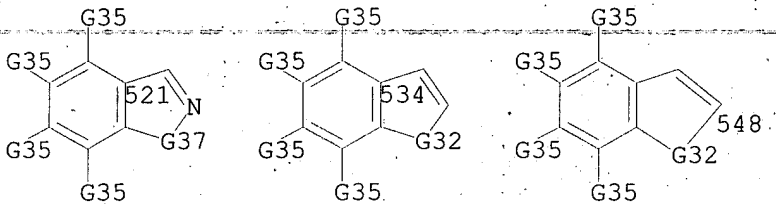










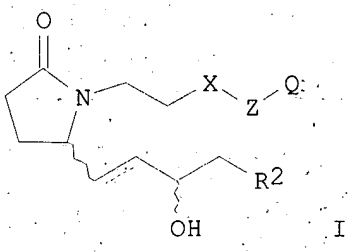


MPL: claim 1
NTE: or salts
NTE: additional heteroatom interruptions and ring formation also claimed

L3 ANSWER 5 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:6083 MARPAT
TITLE: Preparation of EP4 receptor selective agonists for the treatment of osteoporosis
INVENTOR(S): Cameron, Kimberly O'Keefe; Lefker, Bruce Allen
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042268	A2	20020530	WO 2001-IB2073	20011105
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002010848	A5	20020603	AU 2002-10848	20011105
US 2002065308	A1	20020530	US 2001-990556	20011121
PRIORITY APPLN. INFO.:			US 2000-253275P	20001127
			WO 2001-IB2073	20011105

GI

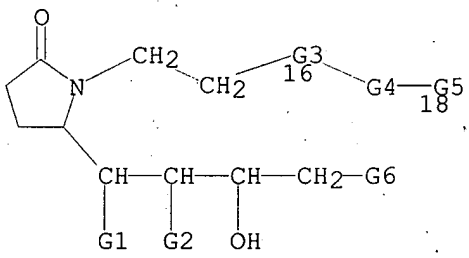


I

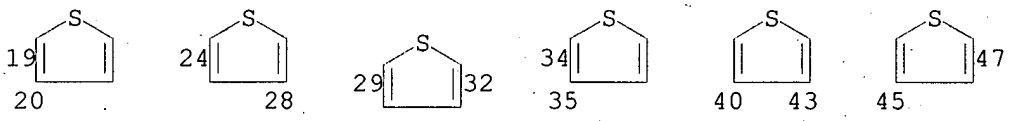
AB This invention is directed to EP4 receptor selective prostaglandin agonists I (e.g. 4-[3-[2-(3-hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propyl]benzoic acid), wherein R2, X, Z and Q are defined below and in more detail in the claims. This invention is also directed to pharmaceutical compns. contg. those compds. This invention is also directed to methods of treating conditions which present with low bone mass, particularly osteoporosis, frailty, an osteoporotic fracture, a bone defect, childhood idiopathic bone loss, alveolar bone loss, mandibular bone loss, bone fracture, osteotomy, bone loss assocd. with periodontitis, or prosthetic ingrowth in a mammal comprising administering those compds. Although biol. testing protocols are included, no test results are given. In I, a prodrug thereof, a pharmaceutically acceptable salt of said compd. or said prodrug or a stereoisomer or diastereomeric mixt. of said compd., prodrug or salt: the dotted line is a bond or no bond; X is -CH2- or O; Z is -(CH2)3-, thienyl, thiazolyl or Ph, provided that when X is O, then Z is phenyl; Q is carboxy, (C1-C4)alkoxycarbonyl or tetrazolyl; R2 is -Ar or -Ar1-V-Ar2; V is a bond, -O-, -OCH2- or -CH2O-. Ar is a partially satd., fully satd. or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, or a bicyclic ring consisting of two fused independently partially satd., fully satd. or fully unsatd. 5-6 membered rings, taken independently, optionally having 1-4 heteroatoms selected independently from N, S and O, said partially or fully satd. ring or bicyclic ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar1 and Ar2 are each independently a partially satd., fully satd. or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, said partially or fully satd. ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar is optionally substituted on C or N, on one ring if the moiety is monocyclic, or on one or both rings if the moiety is bicyclic, with up to three substituents per ring each independently selected from hydroxy, halo, carboxy, (C1-C7)alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8)alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted on C with up to three fluoro. Ar1 and Ar2 are independently optionally substituted on C or N with up to three substituents each independently selected from hydroxy, halo, carboxy, (C1-C7)alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8)alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N-

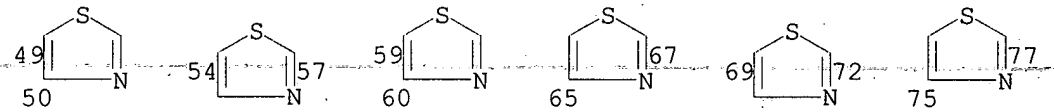
or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar1 and Ar2 are optionally substituted on C with up to three fluoro. (a) when X is (CH2)- and Z is -(CH2)3-, then R2 is not thienyl, Ph or Ph monosubstituted with chloro, fluoro, Ph, methoxy, trifluoromethyl or (C1-C4) alkyl; and (b) when X is (CH2)-, Z is -(CH2)3-, and Q is carboxy or (C1-C4) alkoxycarbonyl, then R2 is not (i) (C5-C7)cycloalkyl or (ii)phenyl, thienyl or furyl each of which may be optionally monosubstituted or disubstituted by one or two substituents selected, independently in the latter case, from halogen atoms, alkyl groups having 1-3 C atoms which may be substituted by one or more halogen atoms, and alkoxy groups having 1-4 C atoms. Although the methods of prepn. are not claimed, 41 example prepns. are included.

MSTR 1

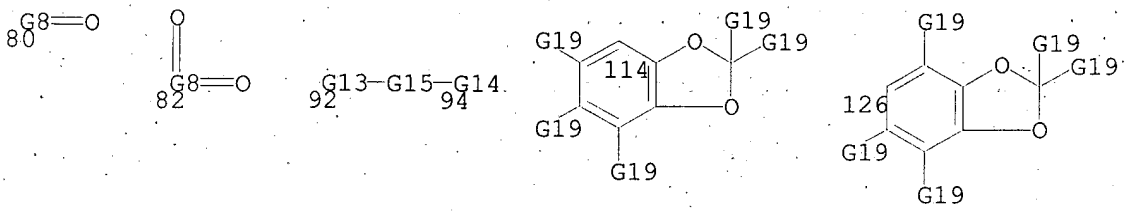


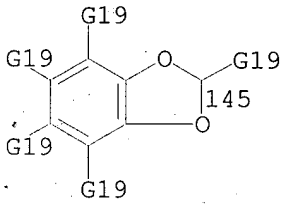
G1 = H
G2 = H
G3 = CH2 / O
G4 = CH2CH2CH2 / phenylene / 19-16 20-18 / 24-16 28-18 / 29-16 32-18 / 35-16 34-18 / 40-16 43-18 / 45-16 47-18 / 49-16 50-18 / 54-16 57-18 / 60-16 59-18 / 65-16 67-18 / 72-16 69-18 / 77-16 75-18



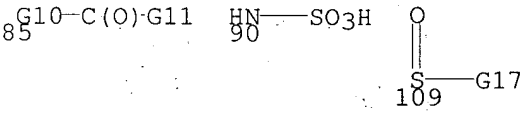


G5 = CO2H / alkoxycarbonyl<(1-4)> / tetrazolyl
G6 = Cb<EC (5-10) C, BD (0-) D, RC (1-2), RS (0-2) E5 (0-2) E6 (0-1) E7 (0-1) E8 (0) OTHER> (SO (1-) G7) / Hy<EC (5-10) A (1-8) Q (0-) N (0-) O (0-) S (0) OTHERQ, BD (0-) D, RC (1-2), RS (0-2) E5 (0-2) E6 (0-1) E7 (0-1) E8 (0) OTHER> (SO (1-) G7) / 80 / 82 / 92 / (SC cyclohexyl (SO (1-2) G18) / thienyl (SO (1-2) G18) / naphthyl (SO (1-2) G18) / Ph (SO (1-3) G20) / 114 / 126 / 145)

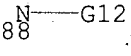




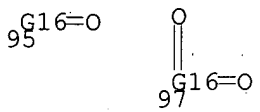
G7 = OH / X / **CO2H** / alkoxy<(1-7)> (SO (1-3) F) / alkyl<(1-4)> (SR alkoxy<(1-4)>) / alkyl<(1-7)> (SO (1-3) F) / alkenyl<(2-7)> / cycloalkyl<(3-7)> / alkyl<(1-4)> (SR cycloalkyl<(3-7)>) / cycloalkylcarbonyl<(3-7)> / alkylcarbonyl<(1-4)> (SR cycloalkyl<(3-7)>) / CHO / alkylcarbonyl<(1-8)> / alkyl<(1-6)> (SR G9) / NHCHO / alkylcarbonylamino<(1-4)> / alkoxycarbonylamino<(1-4)> / SO3H / 85 / 90 / alkylsulfonylamino<(1-4)> / SO2NH2 / alkylaminosulfonyl<(1-4)> / NH2 / alkylamino<(1-4)> / dialkylamino<(1-4)> / CONH2 / alkylaminocarbonyl<(1-4)> / dialkylaminocarbonyl<(1-4)> / CN / SH / alkylthio<(1-6)> / alkylsulfinyl<(1-6)> / alkylsulfonyl<(1-4)> / 109



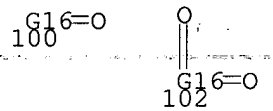
G8 = Cb<EC (5-10) C, BD (0-) D, RC (1-2), RS (0-2) E5 (0-2) E6 (0-1) E7 (0-1) E8 (0) OTHER> (SO (1-) G7) / Hy<EC (5-10) A (1-8) Q (0-) N (0-) O (0-) S (0) OTHERQ, BD (0-) D, RC (1-2), RS (0-2) E5 (0-2) E6 (0-1) E7 (0-1) E8 (0) OTHER> (SO (1-) G7)
G9 = CHO / alkylcarbonyl<(1-6)>
G10 = NH / 88



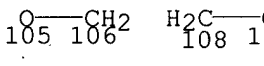
G11 = NH2 / alkylamino<(1-4)> / dialkylamino<(1-4)>
G12 = alkyl<(1-4)>
G13 = **Cb<EC (5-8) C, BD (0-) D, RC (1), RS (1) M5 (1) X8> (SO (1-) G7)** / Hy<EC (5-8) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X8> (SO (1-) G7) / 95 / 97



G14 = **Cb<EC (5-8) C, BD (0-) D, RC (1), RS (1) M5 (1) X8> (SO (1-) G7)** / Hy<EC (5-8) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X8> (SO (1-) G7) / 100 / 102



G15 = NULL / **105-92 106-94** / 108-92 107-94

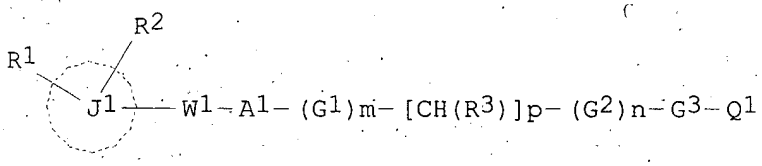


G16 = Cb<EC (5-8) C, BD (0-) D, RC (1), RS (1) M5 (1) X8> (SO (1-) G7) / Hy<EC (5-8) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X8> (SO (1-) G7)
G17 = alkylamino<(1-4)> / dialkylamino<(1-4)>
G18 = alkyl<(1-4)> (SO (1-3) F) / alkoxy<(1-4)> (SO (1-3) F) / alkyl<(1-4)> (SR alkoxy<(1-4)>) / Cl / F / CF3 / CN
G19 = H / alkyl<(1-4)> (SO (1-3) F) / alkoxy<(1-4)> (SO (1-3) F) / alkyl<(1-4)> (SR alkoxy<(1-4)>) / Cl / F / CF3 / CN
G20 = alkyl<(1-4)> (SO (1-3) F) / alkoxy<(1-7)> (SO (1-3) F) / alkyl<(1-4)> (SR alkoxy<(1-4)>) / Cl / F / CF3 / CN / OCF3
G1 +G2 = NULL
MPL: claim 1
NTE: or prodrugs or pharmaceutically acceptable salts
NTE: substitution is restricted
STE: or stereoisomers or diastereomeric mixtures

L3 ANSWER 6 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:355233 MARPAT
TITLE: Preparation of inhibitors for drug efflux pump of Pseudomonas aeruginosa, their use for infectious diseases, and method for screening the inhibitors
INVENTOR(S): Ota, Toshiharu; Nakayama, Kiyoshi
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 23 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002128768	A2	20020509	JP 2000-326655	20001026

PRIORITY APPLN. INFO.: JP 2000-326655 20001026
GI



I

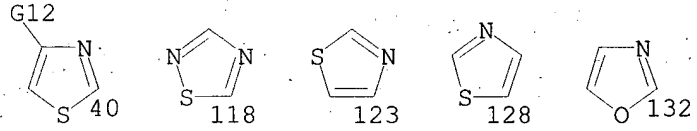
AB The inhibitors, e.g. heterocyclic compds. I [R1, R2 = H, halo, CO2H, etc.; R3 = H, OH, alkoxy; J1 = 5- or 6-membered heterocyclyl; W1 = CH:CH, C.tplbond.C, CH2CH2, OCH2, etc.; A1 = (un)substituted C6H4, (un)substituted pyridinediyl, etc.; G1 = O, CO, CH:N, etc.; p = 0-3; G2 = (un)substituted C6H4, (un)substituted furanidyl, etc.; G3 = CH2, bond; m , n = 0, 1; Q1 = acidic group], their salts, or their hydrates, have 3 hydrophobic and 1 neg. ionizable substructures with specified limited .ANG. values deviated from pharmacophores. The inhibitors are screened using a computer program and/or empirical three-dimensional structural anal. Thus, 3-[(E)-2-(4-phenyl-1,3-thiazol-2-yl)-1-ethenyl]aniline was refluxed with homophthalic anhydride in MePh to give 91% 2-[2-oxo-2-3-[(E)-2-(4-phenyl-1,3-thiazol-2-yl)-1-ethenyl]anilinoethyl]benzoic acid, which at 0.63 .mu.g/mL enhanced the antibacterial activity of levofloxacin against P. aeruginosa PAM 1723.

MSTR 1

G1—G3—G9—G10
1 2 3 4

G1 = **heteroaryl<EC (3-10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (-2) G2)** / (EX 40 / pyridyl / 118 / 2-furyl / 123 / 128 / 132 / 2-thienyl)

G12



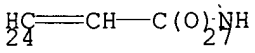
G2 = F / Cl / Br / I / **CO2H** / alkoxycarbonyl<(1-8)> / cycloalkyloxycarbonyl<(3-8)> / NH2 (SO) / alkyl<(1-8)> (SO) / cycloalkyl<(3-8)> (SO) / aryl<(-14)> (SO) / Hy<EC (3-8) A> (SO)

G3 = phenylene (SO) / Hy<EC (5-10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO) / 9-1 10-3

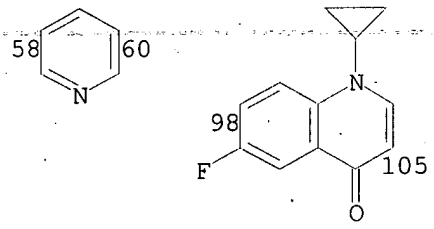
G4—G8
9 10

G4 = CH=CH / ethynylene / CH2CH2 / **11-1 12-10** / 13-1 15-10 / 17-1 18-10 / CH2 / C(O) / CH2CH2CH2 / 19-1 20-10 / 21-1 23-10 / 24-1 27-10

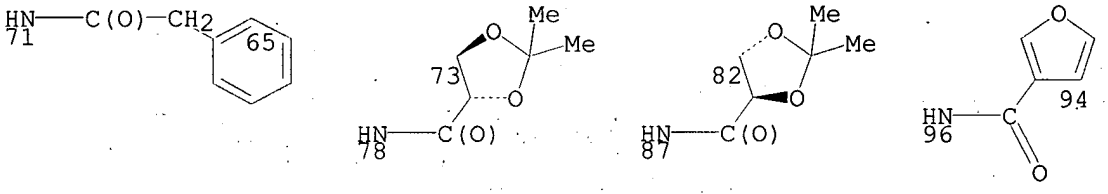
G5—CH2 O—CH2—O H2C—G6 C(O)NH H2C—G7—CH2
11 12 13 15 17 18 19 20 21 23



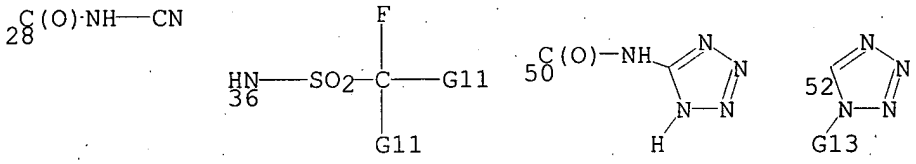
G5 = **O** / S / NH
G6 = O / NH / S
G7 = O / S
G8 = **phenylene (SO)** / Hy<EC (5-10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO) / (EX 58-9 60-3 / 98-9 105-3)



G9 = NULL / R<TX "linking group"> / (EX 71-2 65-4 / 78-2 73-4 / 87-2 82-4 / 96-2 94-4)



G10 = R<TX "acidic group"> / **(EX CO2H** / 28 / 36 / alkoxycarbonyl<(1-8)> (SO) / cycloalkyloxycarbonyl<(3-8)> (SO) / 50 / 52)



G11 = H / F
G12 = Ph / Pr-i
G13 = H / R
MPL: claim 3
NTE: or salts and hydrates
NTE: additional ring formation also claimed

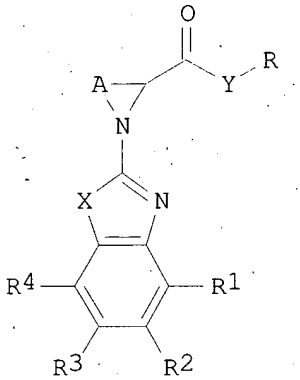
L3 ANSWER 7 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:309922 MARPAT
TITLE: Preparation of benzoxazolyl piperidines and analogs as rotamase enzyme inhibitors
INVENTOR(S): Kemp, Mark Ian; Palmer, Michael John; Sanner, Mark Allen; Wythes, Martin James
PATENT ASSIGNEE(S): Pfizer Inc, USA
SOURCE: U.S., 43 pp.
CODEN: USXXAM

Searched by Barb O'Bryen, STIC 308-4291

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6372736	B1	20020416	US 1999-358107	19990721

PRIORITY APPLN. INFO.: US 1999-358107 19990721
GI



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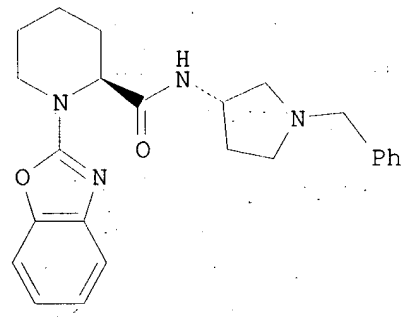
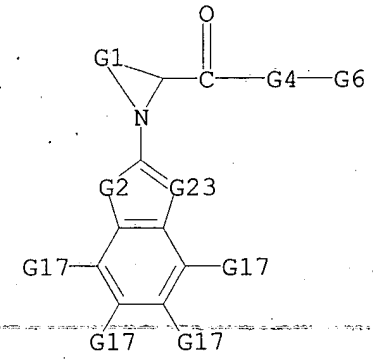


II

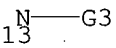
AB Title compds. [I; A = (un)substituted unbranched C3-C5 alkylene; X and Y = independently O, S, NH, or N-alkyl; R = (un)substituted, C-linked, 4- to 6-membered, non-arom., heterocyclic ring contg. 1 N; R1-R4 = independently H, halo, (cyclo)alkyl, haloalkyl, (cyclo)alkoxy, CONR5R6, cycloalkylalkylene, cycloalkylalkoxy, or CO2R7; R5 and R6 = independently H, alkyl, or taken together = unbranched alkylene; R7 = alkyl] were prepd. as rotamase enzyme inhibitors, particularly FKBP-12 and FKBP-52 inhibitors. Thus, (2S)-1-(1,3-benzoxazol-2-yl)-2-piperidinecarboxylic acid (prepn. given) was amidated with (3S)-1-benzylpyrrolidine-3-ylamine in the presence of 1-hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.HCl in CH2Cl2 to yield II. Twenty-one compds. of the invention demonstrated inhibitory activity against human recombinant FKBP-12 in a coupled colorimetric PPIase in vitro assay with IC50 values below 1200 nM, and II inhibited the rotamase enzyme FKBP-52 in a similar assay with IC50 = 2790 nM. As neurotrophic agents, the invention compds. promote neuronal regeneration and outgrowth and are useful for the treatment of neurodegenerative diseases or other disorders involving nerve damage.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1

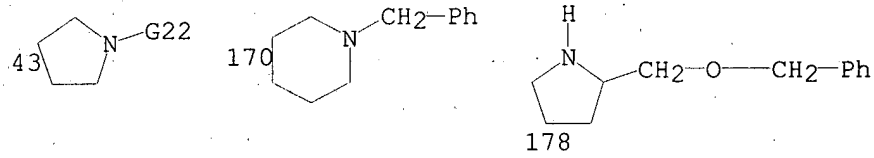


G1 = (3-5) CH2 (SO alkyl<(1-6)>)
G2 = O / S / 13

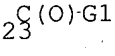


G3 = H / alkyl<(1-6)>
G4 = O / S / NH / 18

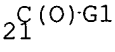
G5 = alkyl<(1-6)>
G6 = Hy<EC (4-6) A (1) Q (1) N (0) OTHERQ (3-5) C, AN (1-) C, RC (1), RS (1) M4 (1) X6> (SO (1-3) G7) / (SC 43 / 170 / 178)



G7 = alkyl<(1-6)> (SO (1-2) G12) / alkenyl<(2-6)> (SO (1-2) G12) / cycloalkyl<(3-7)> / Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / alkoxycarbonyl<(1-6)> / 23



G8 = alkyl<(1-6)> (SO (1-) G25) / alkoxy<(1-6)> / F / Cl / Br / I / **21** / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino



G9 = alkyl<(1-6)> (SO (1-) G25) / alkoxy<(1-6)> / F / Cl / Br / I / Ph / NH2 / alkylamino<(1-6)> /

dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G10 = NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G11 = Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino / Ph (SO (1-3) G8)
G12 = cycloalkyl<(3-7)> / Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / **25** / 29

25 O—G13 29 C(O)G16

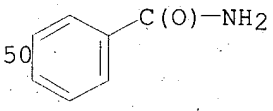
G13 = **Ph (SO (1-3) G8)** / 27

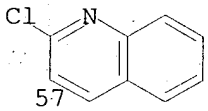
27 G14—G15

G14 = **CH2** / CHMe / CH2CH2
G15 = **Ph (SO (1-3) G8)**
G16 = Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G17 = H / F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G25) / cycloalkyl<(3-7)> / alkoxy<(1-6)> / 35 / cycloalkyloxy<(3-7)> / 37 / 41 / alkoxycarbonyl<(1-6)>

35 C(O)G10 37 G18—G19 41 O—G18—G19

G18 = alkylene<(2-4)>
G19 = cycloalkyl<(3-7)>
G20 = Ph / pyridyl / 50 / 57 / 68 / 83 / 89

50 



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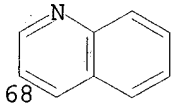

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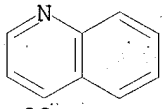

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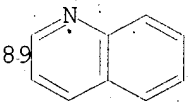
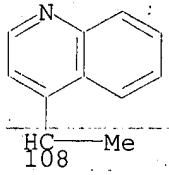


89

G21 = Ph / piperidino / Cl
G22 = 47 / 108 / 120 / 132 / 143 / 156 / 168

47 H2C—G20



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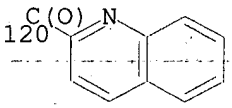

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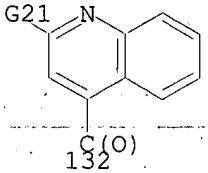

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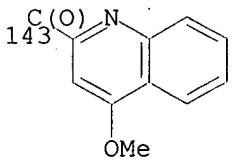

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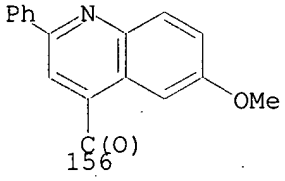

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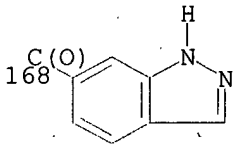
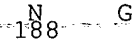


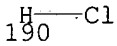
168

G23 = N / 188



188

G24 = R<TX "pharmaceutically acceptable salt"> / (SC 190)



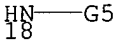
190

G25 = F / Cl / Br / I
MPL: claim 1

MSTR 4

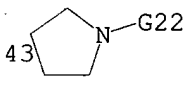
G4—G6

G4 = OH / SH / NH2 / 18



18

G5 = alkyl<(1-6)>
G6 = Hy<EC (4-6) A (1) Q (1) N (0) OTHERQ (3-5) C, AN (1-) C, RC (1), RS (1) M4 (1) X6> (SO (1-3) G7) / (SC 43 / 170 / 178)



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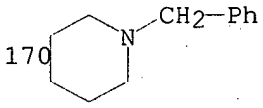

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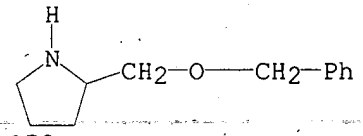
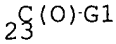


178

G7 = alkyl<(1-6)> (SO (1-2) G12) / alkenyl<(2-6)> (SO (1-2) G12) / cycloalkyl<(3-7)> / Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / alkoxycarbonyl<(1-6)> / 23



23

G8 = alkyl<(1-6)> (SO (1-) G25) / alkoxy<(1-6)> / F / Cl / Br / I / **21** / NH2 / alkylamino<(1-6)> /

dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino

21 C(O)G10

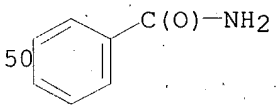
G9 = alkyl<(1-6)> (SO (1-) G25) / alkoxy<(1-6)> / F / Cl / Br / I / Ph / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G10 = NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G11 = Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino / Ph (SO (1-3) G8)
G12 = cycloalkyl<(3-7)> / Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / **25** / 29

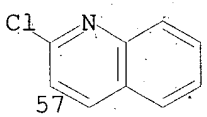
25 O—G13 29 C(O)G16

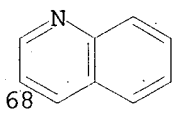
G13 = **Ph (SO (1-3) G8)** / 27

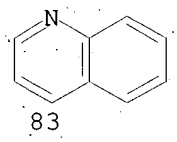
27 G14—G15

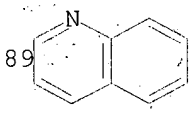
G14 = **CH2** / CHMe / CH2CH2
G15 = **Ph (SO (1-3) G8)**
G16 = Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G20 = Ph / pyridyl / 50 / 57 / 68 / 83 / 89

50 

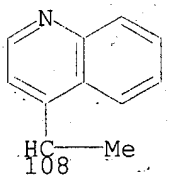
57 

68 

83 

89 

G21 = Ph / piperidino / Cl
G22 = 47 / 108 / 120 / 132 / 143 / 156 / 168

47 H2C—G20 

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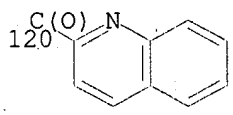
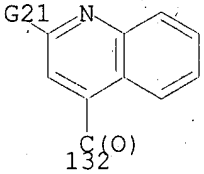
120 



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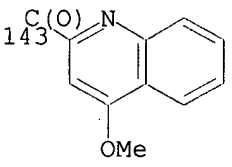
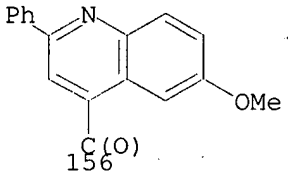
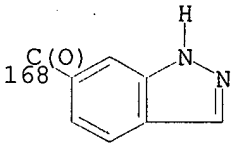






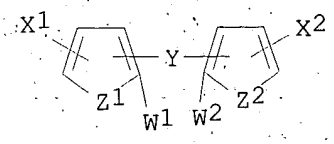
G25 = F / Cl / Br / I
MPL: claim 29

L3 ANSWER 8 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:167374 MARPAT
TITLE: Preparation of (e.g.) pyrrolylalkylphenyl derivatives as histamine H3 antagonists
INVENTOR(S): Bogenstaetter, Michael; Chai, Wenying; Kwok, Annette K.
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012224	A2	20020214	WO 2001-US24654	20010806
WO 2002012224	A3	20020718		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001081119	A5	20020218	AU 2001-81119	20010806
US 2002037896	A1	20020328	US 2001-922622	20010806

PRIORITY APPLN. INFO.: US 2000-223768P 20000808
US 2001-922622 20010806
WO 2001-US24654 20010806

GI



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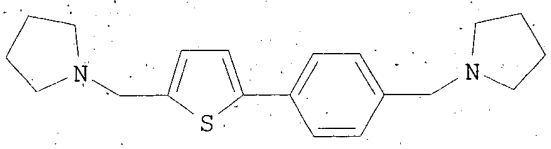
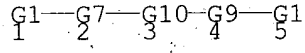


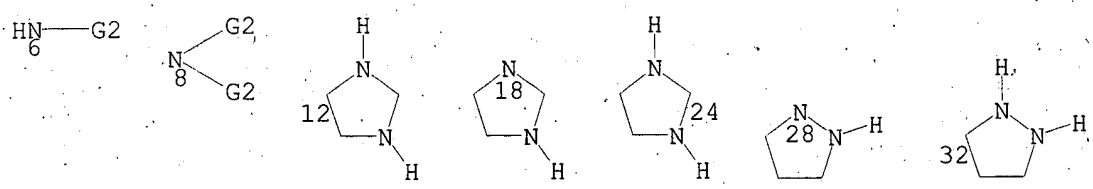
II

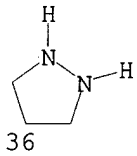
AB Title compds. I [X1 = Ga, RaGa, LaGa, RaLaGa; X2= Gb, RbGb, LbGb, RbLbGb; Ga-b= NR3aR4a or NR3bR4b, resp., or pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperidyl, isoindolinyl, morpholinyl, piperazinyl, imidazolyl, thiazolinyl, 5,6-dihydro-3-imidazo[2,1-b]thiazolyl, thiazolyl; R3a, R4a, R3b, R4b = H, alkyl, cycloalkyl, cycloalkyl-alkyl; Gb can be further selected from NO2, halo, OH, CHO, pyrrolyl, or C(:NOH)H; Ra-b = O, S, NH, C=O; each of La-b = alkylene; Y = covalent bond where one of Z1-2 = N, O, S; Y can also be SO2, C:O, CH2, CH2CH2, OCH2, CH2O, NRc; Rc = H, alkyl, cycloalkyl, cycloalkyl-alkyl, heterocyclyl, heterocyclyl-alkyl, Ph, phenyl-alkyl, or di(alkylamino)-alkyl; Z1-2= N, O, S, CH=CH to form a Ph ring;] were prepd. For instance, 5-formylthiophen-2-ylboronic acid was coupled to 4-bromobenzaldehyde (dioxane, Pd2(dba)3, t-Bu3P, Cs2CO3, 80.degree.C, 24 h) and the product used to reductively alkylate pyrrolidine (CH2Cl2, NaBH(OAc)3, HOAc, 16 h) to give II. II had Ki = 9.0 nM for the histamine H3 receptor. I are useful for treating histamine-mediated disorders, e.g., narcolepsy, sleep disorders, ADHD, etc.

MSTR 1A



G1 = NH2 / 6 / 8 / pyrrolidino / 12 / 18 / 24 / 28 / 32 / 36 / piperidino / 42 / 47 / 58 / 66 / 76 / 78 / 88 / morpholino / 96 / 102 / piperazino / 110 / imidazolyl / 118 / 122 / 131 / 135 / 138 / 142 / 150 / 159 / thiazolyl / NO2 / F / Cl / Br / I / OH / pyrrolyl / CHO / 292 / **294** / 296 / 298 / 301 / 477 / 479 / 481 / 483 / 486 / 489 / (SC 495)





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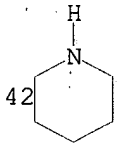

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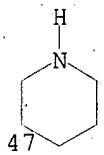

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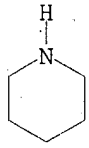

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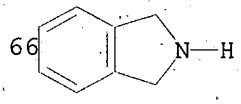

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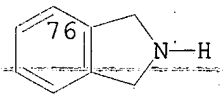

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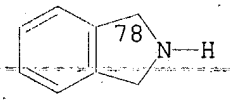

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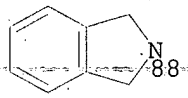

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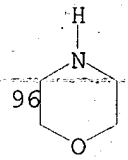

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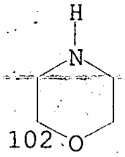

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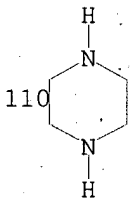

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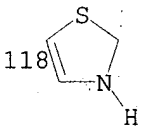

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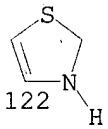

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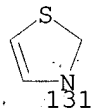

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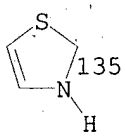

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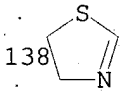

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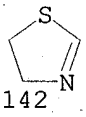

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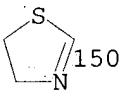

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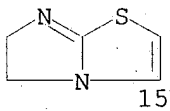


159

G17—G18
292

C(O)G18
294

G4—G18
296

G17—G4—G18
298

C(O)G4—G18
301

G17—G19
477

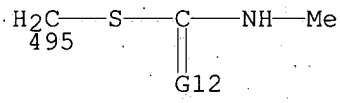
C(O)G19
479

G4—G19
481

G17—G4—G19
483

C(O)G4—G19
486

HC═N—OH
489

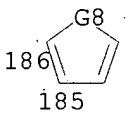


495

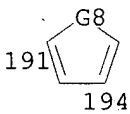
G2 = alkyl<(1-8)> / cycloalkyl<(3-7)> / alkyl<(1-6)> (SR cycloalkyl<(3-7)>) / (SC Me)

G4 = alkylene<(1-3)> / (SC G15)

G7 = 186-1 185-3 / 191-1 194-3 / 196-1 198-3 / 200-1 201-3 / 205-1 209-3 / 210-1 213-3 / **phenylene** / (SC 255-1 257-3)



186
185



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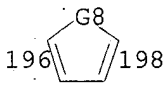

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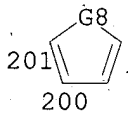

201
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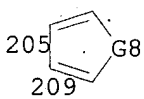
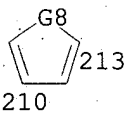
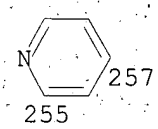
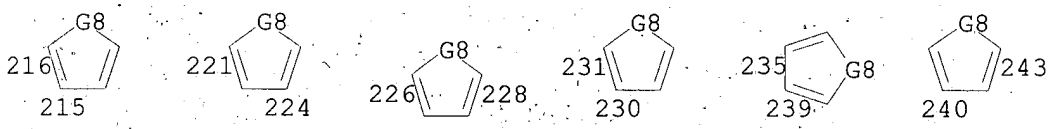
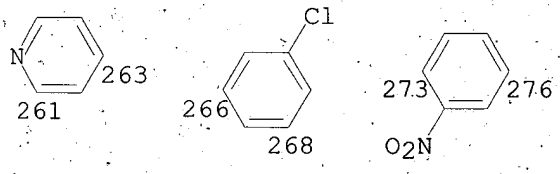




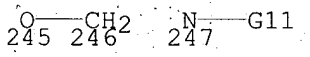


G8 = O / S / NH
G9 = 216-3 215-5 / 221-3 224-5 / 226-3 228-5 /
230-3 231-5 / 235-3 239-5 / 240-3 243-5 / **phenylene** /
(SC 261-3 263-5 / 266-3 268-5 / 273-3 276-5)

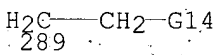




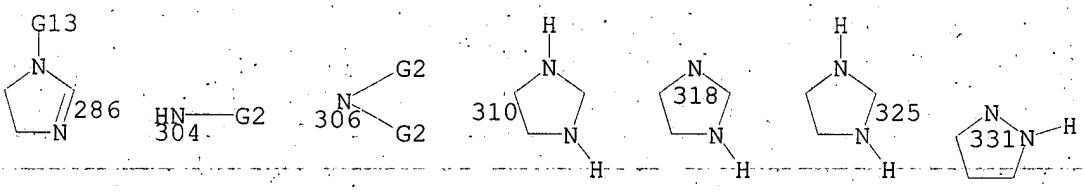
G10 = SO2 / **245-2 246-4** / NH / 247 / C(O) / CH2 / CH2CH2

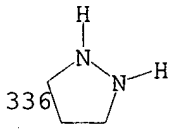


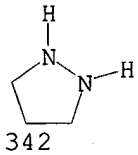
G11 = alkyl<(1-8)> / cycloalkyl<(3-7)> /
alkyl<(1-6)> (SR cycloalkyl<(3-7)>) /
Hy<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ (2-5) C> /
alkyl<(1-6)> (SR Hy<EC (1-) Q (0-) N (0-) O (0-) S (0)
OTHERQ (2-7) C>) / Ph / alkyl<(1-6)> (SR (1-) Ph) /
alkyl<(1-6)> (SR dialkylamino<(1-6)>) / (SC CH2Ph / 289)

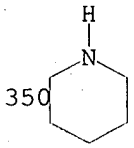


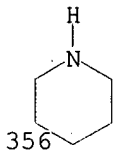
G12 = NMe / NH
G13 = H / Me
G14 = piperidino / NMe2
G15 = (1-3) CH2
G17 = O / S / NH
G18 = NH2 / 304 / 306 / pyrrolidino / 310 / 318 / 325 /
331 / 336 / 342 / piperidino / 350 / 356 / 368 / 377 / 388 /
391 / 402 / morpholino / 410 / 416 / piperazino / 424 /
imidazolyl / 432 / 437 / 447 / 451 / 455 / 459 / 467 / 476 /
thiazolyl / NO2 / F / Cl / Br / I / **OH** / pyrrolyl / (SC 286)

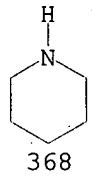


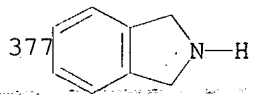


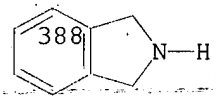


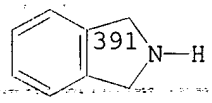


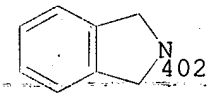


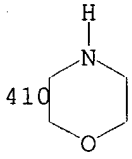


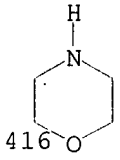


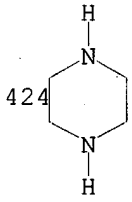


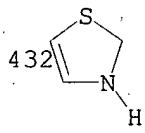


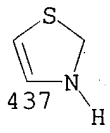


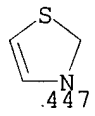


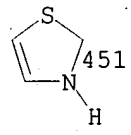


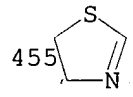


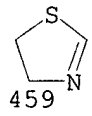


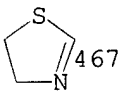


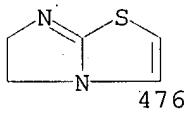




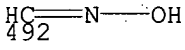








G19 = CHO / 492



MPL: claim 1
NTE: or pharmaceutically acceptable salts, amides, or esters
NTE: substitution is restricted

L3 ANSWER 9 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:135022 MARPAT
TITLE: Preparation of heteroaryl-.beta.-alanine derivatives as antiinflammatory agents and .alpha.4 integrin inhibitors
INVENTOR(S): Konradi, Andrei W.; Pleiss, Michael A.; Thorsett, Eugene D.; Ashwell, Susan; Welmaker, Gregory S.; Kreft, Anthony; Sarantakis, Dimitrios; Dressen, Darren B.; Grant, Francine S.; Semko, Christopher; Xu, Ying-Zi

Searched by Barb O'Bryen, STIC 308-4291

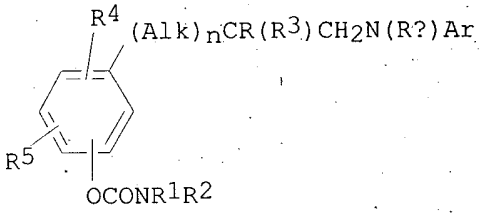
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008222	A2	20020131	WO 2001-US23096	20010720
WO 2002008222	A3	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002086882	A1	20020704	US 2001-910431	20010719

PRIORITY APPLN. INFO.: US 2000-220128P 20000721
GI

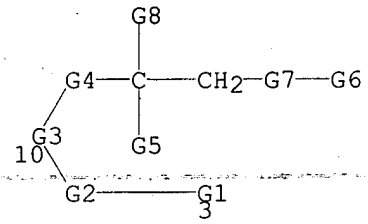


I

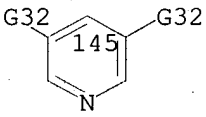
AB Disclosed are a series of heteroaryl-.beta.-alanine derivs. I wherein R is a carboxylic acid; R1 and R2 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, or R1 and R2, together with the nitrogen atom to which they are attached, are joined to form an optionally substituted heterocyclic ring provided that said substituted alkyl, substituted alkenyl and substituted cycloalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; Ra and R3 are independently a hydrogen or a Me group; R4 and R5 are independently selected from the group consisting of heteroatom group; n is zero or an integer 1; Alk is a straight or branched alkylene chain; Ar is an optionally substituted arom. or heteroarom. group, as well as their pharmaceutical use as .alpha.4.beta.7 Integrin inhibitors for the treatment of inflammatory diseases. Thus, 3-[4-(3,5-dichloropyrid-4-ylcarboxamido)phenyl]-2-(3-chlorophenylamino)propanoic acid was prepd. as .alpha.4 Integrin inhibitor. The preferred compds. of the invention generally have IC50 values in the .alpha.4.beta.1 and .alpha.a.beta.7 assays of 1 .mu.M and below. In the other assays featuring .alpha. integrins of other subgroups the same compds. had IC50 values of 50 .mu.M and above thus demonstrating the potency and selectivity of their action against .alpha.4 integrins. Title compds. were prepd. for treating an inflammatory condition in a mammalian patient which condition is mediated by Very Late Antigen 4 (VLA-4). Inflammatory condition is selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, multiple sclerosis,

rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia and acute leukocyte-mediated lung injury.

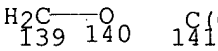
MSTR 1



G1 = **aryl<EC (6-14) C, RC (1-)> (SO (1-3) G9) /** Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (2-10) C, AR (1-), BD (2-) D, RC (1-), RS (0-) E5 (0-) E6> (SO (1-3) G9) / (EX 145)



G2 = NULL / R<TX "bridging group"> / **(EX 139-3 140-10 /** 141-3 142-10)

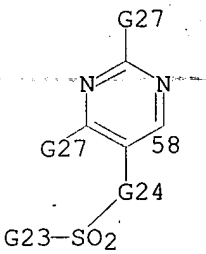


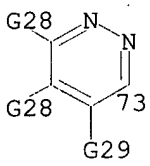
G3 = **Hy<EC (1-4) Q (1-) N (0-) O (0-) S (0) OTHERQ (2-10) C, AR (1-), BD (2-) D, RC (1-), RS (0-) E5 (0-) E6> (SO (1-2) G9)**

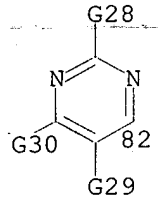
G4 = NULL / alkylene / (EX CH2)

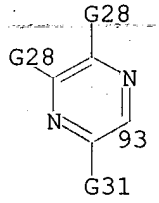
G5 = H / Me

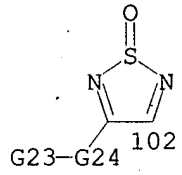
G6 = aryl<EC (6-14) C, RC (1-)> (SO) / Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (2-10) C, AR (1-), BD (2-) D, RC (1-), RS (0-) E5 (0-) E6> (SO) / (SC 58 / 73 / 82 / 93 / 102 / 107)

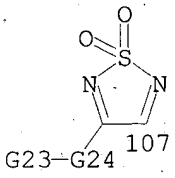




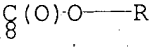




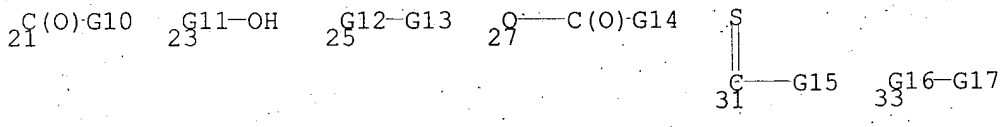


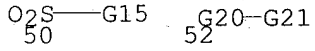


G7 = NH / NMe
G8 = CO2H / 18

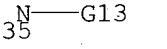


G9 = F / Cl / Br / I / alkyl / OH / alkoxy (SO) / SH / alkylthio (SO) / NH2 / alkylamino (SO) / dialkylamino (SO) / NO2 / CN / **21** / alkylcarbonyl (SO) / SO3H / 23 / 25 / 27 / 31 / 33 / 50 / 52

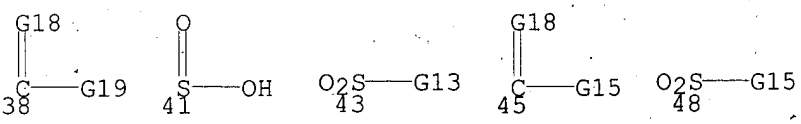




G10 = **OH** / alkoxy (SO) / NH2 / alkylamino (SO) / dialkylamino (SO) / H
G11 = S / S(O)
G12 = S(O) / SO2
G13 = alkyl (SO)
G14 = OH / alkoxy (SO) / H / alkyl (SO)
G15 = NH2 / alkylamino (SO) / dialkylamino (SO)
G16 = NH / 35



G17 = 38 / 41 / 43 / 45 / 48



G18 = O / S
G19 = H / alkyl (SO)
G20 = R<TX "linking group"> / (EX G22 / CHMe / alkylene (SO))
G21 = H / alkyl / F / Cl / Br / I / R
G22 = (1-2) CH2
G23 = alkyl (SO) / alkenyl (SO) / cycloalkyl<EC (3-8) C, RC (1)> (SO) / aryl<EC (6-14) C, RC (1-)> (SO) / cycloalkenyl<(3-8)> (SO) / Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (1-10) C,

BD (0-) D, RC (1-)> (SO)
G24 = NH / 63

N—G25
63

G25 = alkyl (SO) / cycloalkyl<EC (3-8) C, RC (1)> (SO) /
aryl<EC (6-14) C, RC (1-)> (SO) / cycloalkenyl<(3-8)> (SO) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (1-10) C,
BD (0-) D, RC (1-)> (SO) / 65

O_2S—G26
65

G26 = alkyl (SO) / cycloalkyl<EC (3-8) C, RC (1)> (SO) /
cycloalkenyl<(3-8)> (SO) / aryl<EC (6-14) C, RC (1-)> (SO) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (1-10) C,
BD (0-) D, RC (1-)> (SO)
G27 = H / alkyl (SO) / cycloalkyl<EC (3-8) C, RC (1)>
(SO) / aryl<EC (6-14) C, RC (1-)> (SO) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (1-10) C,
BD (0-) D, RC (1-)> (SO) / F / Cl / Br / I
G28 = H / alkyl (SO) / alkoxy (SO) / NH2 (SO) /
cycloalkyl<EC (3-8) C, RC (1)> (SO) /
aryl<EC (6-14) C, RC (1-)> (SO) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (1-10) C,
BD (0-) D, RC (1-)> (SO) / F / Cl / Br / I
G29 = alkyl (SO) / alkoxy (SO) / NH2 (SO) /
cycloalkyl<EC (3-8) C, RC (1)> (SO) /
aryl<EC (6-14) C, RC (1-)> (SO) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (1-10) C,
BD (0-) D, RC (1-)> (SO)
G30 = H / alkyl (SO) / alkoxy (SO) /
cycloalkyl<EC (3-8) C, RC (1)> (SO) /
aryl<EC (6-14) C, RC (1-)> (SO) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (1-10) C,
BD (0-) D, RC (1-)> (SO) / F / Cl / Br / I
G31 = alkyl (SO) / alkoxy (SO) / NH2 (SO) /
cycloalkyl<EC (3-8) C, RC (1)> (SO) /
aryl<EC (6-14) C, RC (1-)> (SO) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (1-10) C,
BD (0-) D, RC (1-)> (SO)
G32 = H / F / Cl / Me / CF3 / 151 / 153 / OMe / 155 / 158

H_2C—F 151 F_2C—H 153 O—CH_2—F 155 O—CF_2—H 158

MPL: claim 1
NTE: and salts, solvates, hydrates, or N-oxides

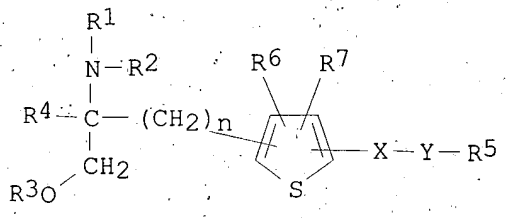
L3 ANSWER 10 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:134664 MARPAT
TITLE: Preparation of aminoalkanol moiety-containing thiophene derivatives as immunosuppressants
INVENTOR(S): Nishi, Takahide; Takemoto, Toshiyasu; Shimozato, Takaichi; Nara, Futoshi
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: PCT Int. Appl., 373 pp.
CODEN: PIXXD2

Searched by Barb O'Bryen, STIC 308-4291

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006268	A1	20020124	WO 2001-JP5988	20010710
W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RU, SG, SK, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
JP 2002167382	A2	20020611	JP 2001-211778	20010712
PRIORITY APPLN. INFO.:			JP 2000-212246	20000713
			JP 2000-241744	20000809
			JP 2000-283218	20000919

GI

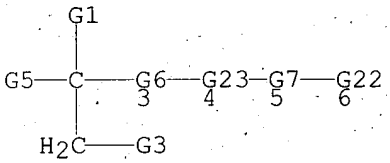


I

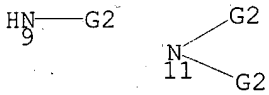
AB The title compds. I [R1 and R2 are each hydrogen or an amino-protecting group; R3 is hydrogen or a hydroxyl-protecting group; R4 is lower alkyl; n is an integer of 1 to 6; X is ethylene, etc.; Y is (un)substituted C1-10 alkylene, etc. ; R5 is aryl, etc.; and R6 and R7 are each hydrogen, alkyl, etc.; a proviso is given] are prepd. Processes for prepg. intermediates for I are claimed. (2R)-Amino-2-methyl-4-[5-[3-(4-methylphenoxy)propynyl]thiophen-2-yl]butan-1-ol maleic acid salt showed oral ID50 of 0.04 mg/kg against adjuvant arthritis in rats.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1

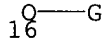


G1 = NH2 / 9 / 11

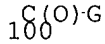


G2 = R<TX "protecting group"> /
(SC alkoxycarbonyl<(1-6)> / alkoxycarbonyl (SR (1-) G26))

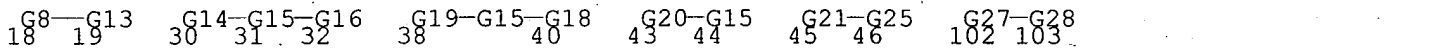
G3 = OH / 16

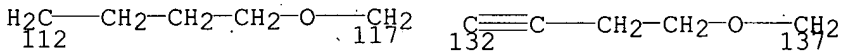


G4 = R<TX "protecting group"> / (SC alkyl<(1-6)> / 100 / arylcarbonyl<(6-10)> (SO (1-3) G9))

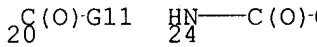


G5 = alkyl<(1-6)> / (SC Me / Et)
G6 = (1-6) CH2
G7 = 18-4 19-6 / arylene<(6-10)> (SO (1-3) G9) / Ak<EC (2-12) C, BD (-1) D (-1) T> (SO (1-3) G12) / 30-4 32-6 / 38-4 40-6 / 43-4 44-6 / 45-4 46-6 / (SC 102-4 103-6 / 112-4 117-6 / 132-4 137-6)

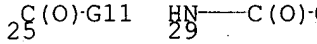




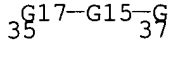
G8 = C(O) / CHOH / O / S / NH
G9 = F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G10) / alkoxy<(1-6)> / alkylthio<(1-6)> / **CO2H** / alkoxycarbonyl<(1-6)> / OH / 20 / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / 24 / CN / NO2



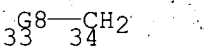
G10 = F / Cl / Br / I
G11 = H / Ak<(1-6)>
G12 = F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G10) / alkoxy<(1-6)> / alkylthio<(1-6)> / **CO2H** / alkoxycarbonyl<(1-6)> / OH / 25 / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / 29 / CN / NO2 / cycloalkyl<(3-10)> (SO) / aryl<(6-10)> (SO) / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RS (0-) E5 (0-) E6 (0-) E7 (0) OTHER> (SO)



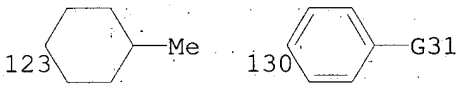
G13 = alkylene<(1-11)> (SO (1-3) G12) / 35-18 37-6 / 41-18 42-6



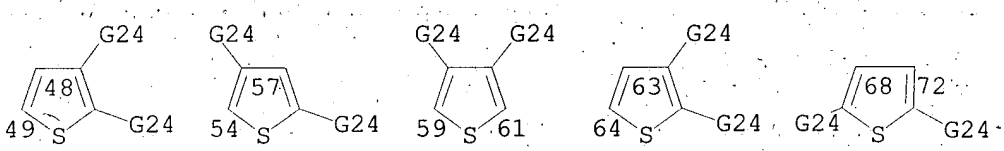
G14 = CH2CH2 / CH=CH / ethynylene / 33-4 34-31 / arylene<(6-10)> (SO (1-3) G9)

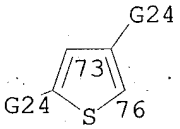


G15 = O / S
G16 = alkylene<(1-10)> (SO (1-3) G12)
G17 = alkylene<(2-10)> (SO (1-3) G12)
G18 = alkylene<(1-9)> (SO (1-3) G12)
G19 = Ak<EC (3-11) C, BD (-1) D (-1) T> (SO (1-) G12) / arylene<(6-10)> (SO (1-3) G12)
G20 = Ak<EC (3-11) C, BD (-1) D (-1) T> (SO (1-) G12)
G21 = arylene<(6-10)> (SO (1-3) G9)
G22 = H / cycloalkyl<(3-10)> (SO (1-3) G12) / **aryl<(6-10)> (SO (1-3) G12)** / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RS (0-) E5 (0-) E6 (0-) E7 (0) OTHER> (SO (1-3) G12) / (SC cyclohexyl / Ph (SO (1-3) G30) / 123 / 130)

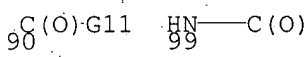


G23 = 49-3 48-5 / 54-3 57-5 / 59-3 61-5 / 63-3 64-5 / 68-3 72-5 / 73-3 76-5

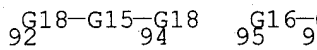




G24 = H / F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G10) / alkoxy<(1-6)> / alkylthio<(1-6)> / CO2H / alkoxycarbonyl<(1-6)> / OH / 90 / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / 99 / CN / NO2



G25 = alkylene<(1-10)> (SO (1-) G12) / 92-45 94-6 / 95-45 96-6



G26 = aryl (SO (1-3) G9)
G27 = CH2CH2 / CH=CH / ethynylene / 104-4 105-103 / **arylene<(6-10)> (SO (1-3) G9)**

G8—CH2
104 105

G28 = CH2CH2 / CH2CH2CH2 / CH2CH2CH2CH2 / **106-102 107-6** /
109-102 108-6

O—G29 G29—O
106 107 109 108

G29 = **(1-3) CH2**
G30 = F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G10) /
alkoxy<(1-6)> / 110 / Me / CF3 / OMe / COMe

C(O)G11
110

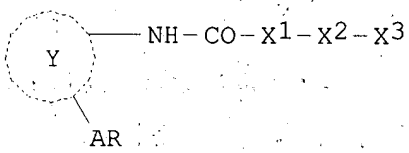
G31 = Et / SMe
MPL: claim 1
NTE: or pharmacologically acceptable salts or esters
NTE: additional heteroatom interruptions also claimed
NTE: substitution is restricted

L3 ANSWER 11 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:37614 MARPAT
TITLE: Preparation of chiral heterocyclylcarbonylaminobicyclo heptanehydrocarboncarboxylic acids in remedy composition antagonistic to both PGD2 and TXA2 receptors
INVENTOR(S): Tanimoto, Norihiko; Arimura, Akinori
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 278 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

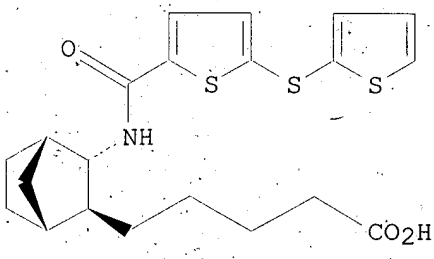
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094309	A1	20011213	WO 2001-JP4430	20010528

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-166305 20000602
GI



I

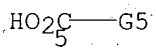


II

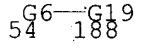
AB Title compds. [I; A = alkylene optionally having an unsatd. bond; R = COR1, CH2OCH3, CH2OH; R1 = OH, OCH3, NH2, NHSO2CH3; X1, X3 independently = optionally substituted aryl, optionally substituted heteroaryl; X2 = single bond, CH2, S, SO2, CH2O, OCH2, CH2S, SCH2; Y = bicycloheptane] and pharmaceutically acceptable salts or solvates, having antagonistic effect on both thromboxane A2 and prostaglandin D2 receptors, are prepd. Thus, the title compd. II was prepd. and biol. tested for TXA2 receptor antagonistic activity with IC50(.mu.M) = 0.011 and PGD2 receptor antagonistic activity with IC50(.mu.M) = 0.079.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

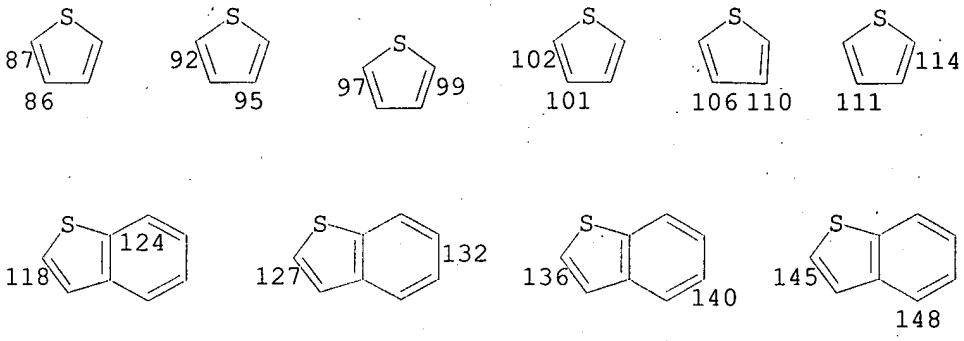
MSTR 2

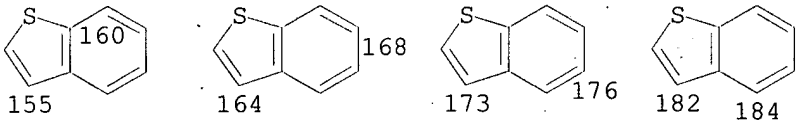


G5 = 54 / aryl<RC (3-)> (SO) / heteroaryl<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (3-)> (SO) / Hy<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, AR (0), RC (3-)> (SO)

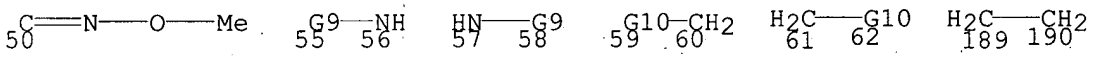


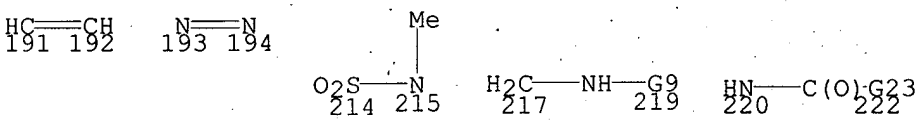
G6 = arylene<RC (1-)> (SO) / **heteroarylene<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-)> (SO)** / Hy<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, AR (0), RC (1-)> (SO) / (SC 87-5 86-188 / 92-5 95-188 / 97-5 99-188 / 101-5 102-188 / 106-5 110-188 / 111-5 114-188 / 118-5 124-188 / 127-5 132-188 / 136-5 140-188 / 145-5 148-188 / 155-5 160-188 / 164-5 168-188 / 173-5 176-188 / 182-5 184-188 / Hy<EC (1) Q (1) S (8) C, AR (1-), BD (6) N (1) D, FA (2) C, RC (2), RS (1) E5 (1) E6> (SO) / Hy<EC (1) Q (1) S (4) C, AR (1-), BD (2) D, RC (1), RS (1) E5> (SO))



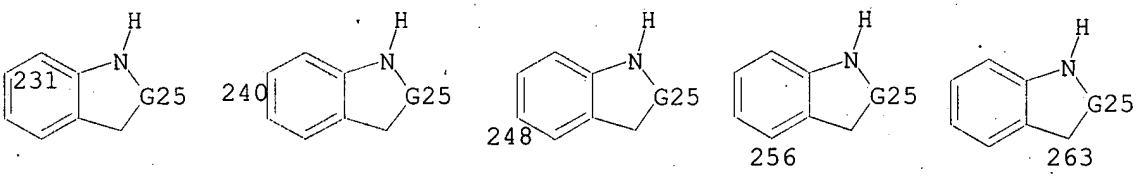


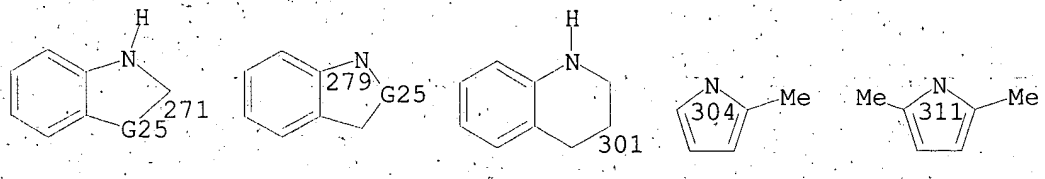
G7 = CH2 / 189-54 190-49 / C(O) / O / S / S(O) / SO2 / NH / NMe / 50 / 191-54 192-49 / 193-54 194-49 / 55-54 56-49 / 57-54 58-49 / **59-54 60-49** / 61-54 62-49 / C=CH2 / 214-54 215-49 / 217-54 219-49 / 220-54 222-49



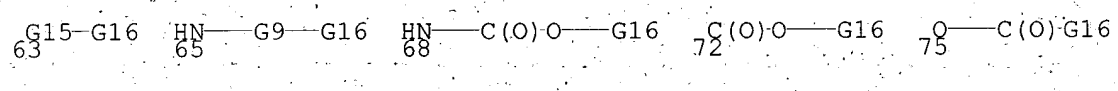


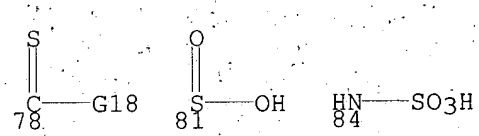
G8 = aryl<RC (1-)> (SO (1-3) G11) / **heteroaryl<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-)> (SO (1-3) G11)** / Hy<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, AR (0), RC (1-)> (SO) / (SC thienyl (SO) / benzothienyl (SO) / pyrrolyl (SO (1-) G24) / indolyl (SO (1-) G24) / 231 / 240 / 248 / 256 / 263 / 271 / 279 / 301 / Hy<EC (9-10) A (1) Q (1) N (0) OTHERQ, AR (1-), BD (3) D, FA (2) C, RC (2), RS (0-1) E5 (1-2) E6 (0) OTHER> (SO (1-) G24) / 304 / 311)



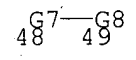


G9 = C(O) / SO2
G10 = NH / O / S / SO2
G11 = alkyl<(1-8)> (SO (1-) G12) / cycloalkyl<(3-8)> (SO (1-) G12) / alkenyl<(2-8)> / cycloalkenyl<(3-8)> / alkynyl<(2-8)> / aryl<RC (1-)> (SO (1-) G13) / heteroaryl<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G13) / alkyl<(1-8)> (SR (1-) G14) / cycloalkyl<(3-8)> (SR (1-) G14) / 63 / 65 / 68 / 72 / 75 / **CO2H** / F / Cl / Br / I / alkyl<(1-8)> (SR (1-2) OH) / cycloalkyl<(3-8)> (SR (1-2) OH) / OH / NO2 / CN / SH / 78 / 81 / SO3H / SO2NH2 / 84 / NH2 (SO) / alkyl<(1-8)> (SR NH2 (SO)) / cycloalkyl<(3-8)> (SR NH2 (SO)) / NHOH / CONH2 / NHNH2





G12 = F / Cl / Br / I
G13 = alkyl<(1-8)> / cycloalkyl<(3-8)> / F / Cl / Br / I
G14 = aryl<RC (1-)> (SO (1-) G13) / heteroaryl<EC (1-) Q (0-) N (0-) S (0-) O (0) OTHERQ> (SO (1-) G13)
G15 = O / S / NH / C(O) / SO2
G16 = alkyl<(1-8)> (SO (1-) G12) / cycloalkyl<(3-8)> (SO (1-) G12) / alkenyl<(2-8)> / cycloalkenyl<(3-8)> / alkynyl<(2-8)> / aryl<RC (1-)> (SO (1-) G13) / heteroaryl<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G13) / alkyl<(1-8)> (SR (1-) G14) / cycloalkyl<(3-8)> (SR (1-) G14)
G18 = H / Me / OH / SH / NH2
G19 = aryl<RC (1-)> (SO) / heteroaryl<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-)> (SO) / Hy<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, AR (0), RC (1-)> (SO) / 48 / (SC thienyl (SO) / benzothienyl (SO))

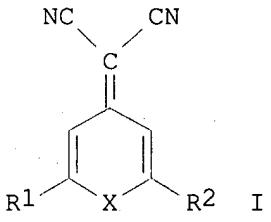


G23 = NH / NMe
G24 = alkyl<(1-8)> / cycloalkyl<(3-8)> / alkoxy<(1-8)> / cycloalkyloxy<(3-8)> / F / Cl / Br / I
G25 = (1-2) CH2
MPL: claim 23

L3 ANSWER 12 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:378558 MARPAT
TITLE: Organic electroluminescent component
INVENTOR(S): Abiko, Hiroshi; Murayama, Tatsushi
PATENT ASSIGNEE(S): Tohoku Pioneer Corporation, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 25 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001326080	A2	20011122	JP 2000-146670	20000518

PRIORITY APPLN. INFO.: JP 2000-146670 20000518
GI



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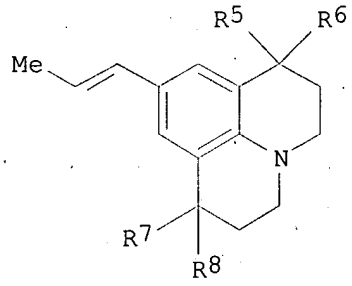


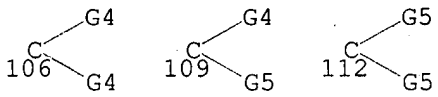
II

AB The invention refers to an org. electroluminescent component with white electroluminescence comprising a guest-host material wherein the guest material is a dicyanomethylene pyran compd. I [X = O or S; R1 = C1-10 alkyl, or C6 or C10 aryl, R2 = CH3CH:CH-Ph-NR3R4, or II; R3,8 = H, C1-4 alkyl].

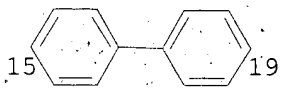
MSTR 2

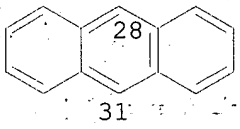
G1=CH(8)—G2—CH(9)=G1

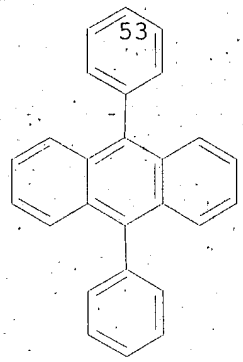
G1 = 106 / 109 / **112** / Cb<BD (0-) D, RS (0-) E5 (0-) E6> / Hy<BD (0-) D, RS (0-) E5 (0-) E6>



G2 = arylene<(6-20)> (SO) / 114-8 115-9 / 116-8 118-9 / phenylene (SO) / Cb<BD (0-) D, RS (0-) E5 (0-) E6> / Hy<BD (0-) D, RS (0-) E5 (0-) E6> / (EX 15-8 19-9 / 31-8 28-9 / 59-8 53-9)



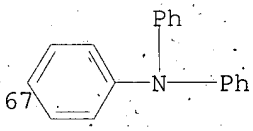


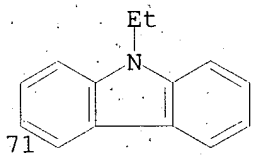


G6—G6
114 115

G6—G6—G6
116 118

G3 = alkyl<(1-6)> / alkoxy<(1-6)> /
alkyl<(1-)> (SR (1-) aryl<(6-)>) / aryloxy<(6-18)> / CHO /
alkylcarbonyl<(1-6)> / OCHO / acyl / acyloxy /
alkylcarbonyloxy<(1-6)> / **CO2H** / CH=CHPh /
arylcarbonyl<(6-20)> / aryloxycarbonyl<(6-20)> /
alkoxycarbonyl<(1-6)> / CH=CH2 / CONHPh / CONH2 / Ph / NO2 /
OH / X
G4 = alkyl<(1-)> (SR aryl<(6-)>) / alkyl<(1-6)>
G5 = H / alkoxy<(1-6)> / **aryl<(6-18)> (SO (1-) G3)** /
heteroaryl (SO (1-) G3) / cyclohexyl (SO) /
aryloxy<(6-18)> (SO (1-) G3) / naphthyl / biphenylyl /
(EX 67 / 71)





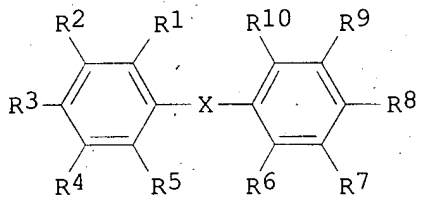
G6 = arylene<(6-20)> (SO)
MPL: claim 4
NTE: additional ring formation also claimed
NTE: substitution is restricted

L3 ANSWER 13 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:371527 MARPAT
TITLE: Preparation of bisacylguanidine with cardioprotective activity
INVENTOR(S): Gericke, Rolf; Beier, Norbert
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

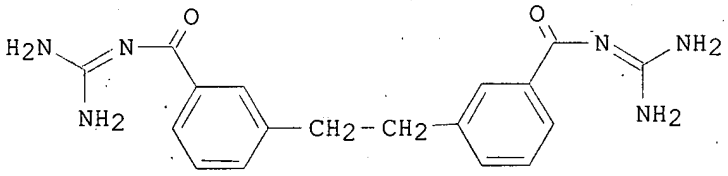
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 10024319 A1 20011122 DE 2000-10024319 20000517
WO 2001087829 A1 20011122 WO 2001-EP4425 20010419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: DE 2000-10024319 20000517
OTHER SOURCE(S): CASREACT 135:371527

GI



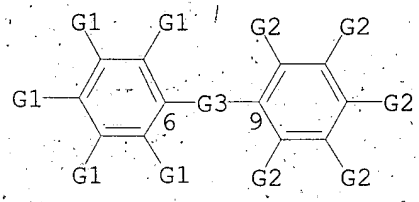
I



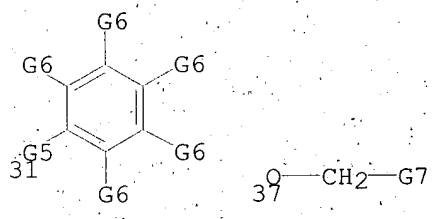
II

AB Bisacylguanidines I [one of R1, R2, R3, R4 or R5 = CON:C(NH2)2, CH:CMeCON:C(NH2)2 and one of R6, R7, R8, R9 or R10 = CON:C(NH2)2, CH:CMeCON:C(NH2)2; the other R1 - R10 = H, A, CH, F, Cl, Br, I, SA, OA, SO2A, OH, NH2, NHA, NA2, COA, (un)substituted Ph, CH2Ph, OPh, N-, S-, O-contg. heterocycle; X = S, SO2, (CH2)n, CO,O, OCH2; A = C1-8-alkyl; n = 1 - 3] and their physiol. harmless salts and/or solvates, with cardioprotective characteristics and works as inhibitors of the cellular Na+/H+ antiporters of the Subtyp 1 are described. Thus, N-{3-[2-(3-guanidinocarbonylphenyl)ethyl]benzoyl}guanidine dihydrochloride (II.cntdot.HCl), was prepd. from 3-[2-(3-carboxyphenyl)ethyl]benzoic acid and Boc-guanidine in 1-methyl-2-pyrrolidone contg. 2-chloro-1-methylpyridinium iodide and Et2NCHMe2, followed by hydrolysis with aq. HCl. Formulations for use in injections, suppositories, solns., tablets, capsules and ampules are given.

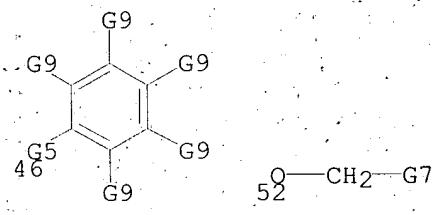
MSTR 1



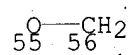
G1 = (1) G4 / H / alkyl<(1-8)> / CN / F / Cl / Br / I / alkylthio<(1-8)> / alkoxy<(1-8)> / alkylsulfonyl<(1-8)> / Ph (SO (1-3) G8) / 31 / 37 / Hy<EC (1-2) Q (0-) N (0-) O (0-) S> (SO (1-) G12) / NH2 (SO (1-2) alkyl<(1-8)>) / alkylcarbonyl<(1-8)>



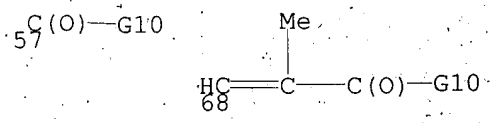
G2 = (1) G4 / H / alkyl<(1-8)> / CN / F / Cl / Br / I / alkylthio<(1-8)> / alkoxy<(1-8)> / alkylsulfonyl<(1-8)> / Ph (SO (1-3) G8) / 46 / 52 / Hy<EC (1-2) Q (0-) N (0-) O (0-) S> (SO (1-) G12) / NH2 (SO (1-2) alkyl<(1-8)>) / alkylcarbonyl<(1-8)>



G3 = S / SO2 / CH2 / CH2CH2 / CH2CH2CH2 / C(O) / O / **55-6 56-9**

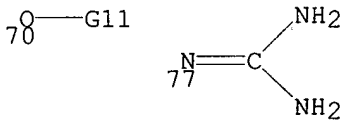


G4 = **57** / 68

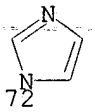


G5 = O / CH2
G6 = (3-) H / alkyl<(1-8)> / alkoxy<(1-8)> / NH2 (SO (1-2) alkyl<(1-8)>) / F / Cl / Br / CF3
G7 = Ph (SO (1-3) G8)
G8 = alkyl<(1-8)> / alkoxy<(1-8)> / NH2 (SO (1-2) alkyl<(1-8)>) / F / Cl / Br / CF3
G9 = (3-) H / alkyl<(1-8)> / alkoxy<(1-8)> / NH2 (SO (1-2) alkyl<(1-8)>) / F / Cl / Br / CF3

G10 = 77 / Cl / Br / I / **OH** / 70



G11 = R<TX "reactive group"> / (EX 72 / alkylsulfonyl<(1-6)> / SO2Me / arylsulfonyl<(6-10)> / SO2Ph / SO2C6H4Me-p)



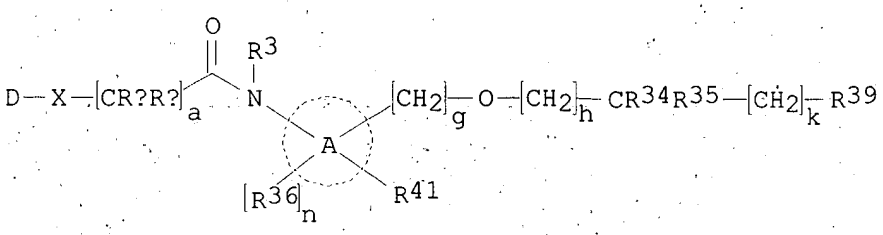
G12 = F / Cl / Br / I / alkyl<(1-8)> / alkoxy<(1-8)> / alkoxycarbonyl<(1-8)> / CN / CO2H
MPL: claim 1
NTE: and physiologically acceptable salts and/or solvates
NTE: also incorporates claim 3

L3 ANSWER 14 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:137405 MARPAT
TITLE: Preparation of substituted diphenyl ureas as inhibitors for VLA-4
INVENTOR(S): Johnstone, Craig; Large, Michael Stewart
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053279	A1	20010726	WO 2001-GB162	20010117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1252152	A1	20021030	EP 2001-900551	20010117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: GB 2000-1348 20000121
WO 2001-GB162 20010117

GI



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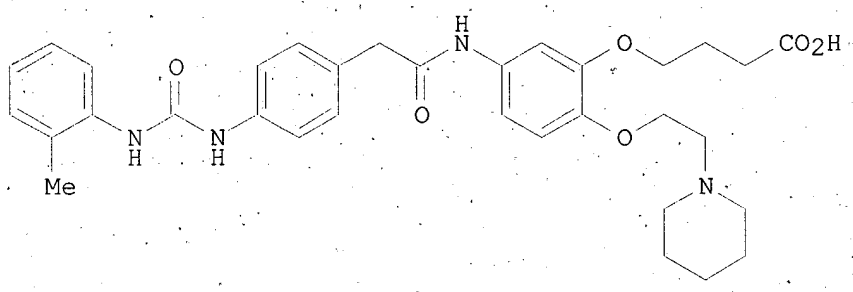
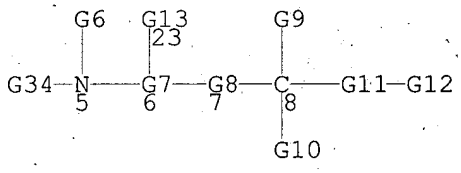


II

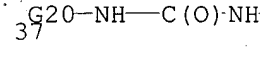
AB The title compds. [I; D = a VLA-4 specificity determinant which does not impart significant IIB/IIIa activity; Ra, Rb = H, alkyl; a = 1-4; X = a bond, O, S, etc.; R3 = H, alkyl; A = aryl, heterocyclyl; n = 0-3; R34 = H, alkyl, aryl, etc.; R35 = H, OH, alkyl, etc.; R36 = alkyl, alkenyl, alkoxy, etc.; R39 = an acidic functional group; h = 0-1; g = 0-1; k = 0-3; R41 = U(CH2)dVT (wherein U = O, S, a bond, CH2O; V = N, O, S, etc.; d = 0-4; T = H, alkyl, alkoxy, etc.)], useful in the treatment of disease mediated by the interaction between VCAM-1 and/or fibronectin and the integrin receptor .alpha.4.beta.1 (such as hypersensitivity and arthritis), were prepd. E.g., a multi-step synthesis of the urea II which was found to be an inhibitor at 87 nM in MOLT-4 cell/Fibronectin adhesion assay, was given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1

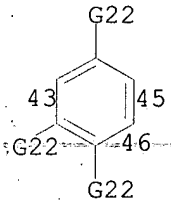


G1 = R<TX "VLA-4 specificity determinant"> / (SC 37)

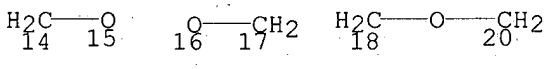


G2 = O / S / NH / 11 / NULL

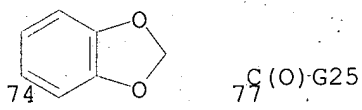
G3 = alkyl<(1-4)>
G4 = alkylene<(1-)> / G5
G5 = (1-4) CH2
G6 = H / alkyl<(1-5)>
G7 = **Cb<EC (6-) C, AR (1-), BD (6-) N, RS (1-) E6> (SO (1-3) G29)** / Hy<EC (-5) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-3) G29) / (SC 43-5 45-7 46-23)



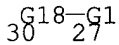
G8 = 14-6 15-8 / 16-6 17-8 / 18-6 20-8



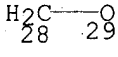
G9 = H / R
G10 = H / OH / Ak<EC (1-6) C, BD (0-) D (0) T> / 74 / 77 / Hy<EC (-5) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G30) / aryl (SO (1-) G30)



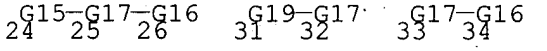
G11 = (0-3) CH2
G12 = R<TX "acidic functional group"> / (EX CO2H)
G13 = H / alkyl<(1-)> (SO (1-) G26) / alkoxy<(1-4)> / cycloalkyl<(3-7)> / aryl / Hy<EC (-3) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G28) / 30



G14 = H / alkyl<(1-10)> (SO (1-) G26) / alkoxy<(1-4)> / cycloalkyl<(3-7)> / aryl / **Hy<EC (-3) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G28)**
G15 = O / S / 28-6 29-25



G16 = NH (SO) / O / S / S(O) / SO2
G17 = **(1-4) CH2**
G18 = 24-6 26-27 / 31-6 32-27 / 33-6 34-27 / 91-6 92-27 / O / S / NH (SO) / S(O) / SO2 / G17



G19 = O / S / 35-6 36-32

G20 = p-C6H4 (SO (1-) G23)
G21 = Ph (SO (1-) G31)
G22 = H / alkyl<(1-6)> / alkenyl<(2-6)> / alkynyl<(2-6)> / alkoxy<(1-4)> / CHO / alkylcarbonyl<(1-4)> / alkylamino<(1-6)> / alkyl<(1-6)> (SR alkoxy<(1-4)>) / alkyl<(1-6)> (SR alkylamino<(1-6)>) / NO2 / CN / F / Cl / Br / I / CF3 / OH / CH2OH / CH2CH2OH / 81

G23 = R / alkoxy<(1-4)>
G25 = 79 / NH2 (SO)

G26 = alkoxy<(1-4)> / aryl
G27 = **OH** / alkoxy<(1-6)> / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)>
G28 = alkyl<(1-6)> / alkenyl<(2-6)> / alkynyl<(2-6)> / alkoxy<(1-6)> / CHO / alkylcarbonyl<(1-4)> / alkylamino<(1-6)> / alkyl<(1-6)> (SR alkoxy<(1-6)>) / alkyl<(1-6)> (SR alkylamino<(1-6)>) / alkylsulfonyl<(1-4)> / NO2 / CN / F / Cl / Br / I / CF3 / OH / CH2OH / CH2CH2OH / **83**

G29 = alkyl<(1-6)> / alkenyl<(2-6)> / alkynyl<(2-6)> / alkoxy<(1-4)> / CHO / alkylcarbonyl<(1-4)> / alkylamino<(1-6)> / alkyl<(1-6)> (SR alkoxy<(1-4)>) / alkyl<(1-6)> (SR alkylamino<(1-6)>) / NO2 / CN / F / Cl / Br / I / CF3 / OH / CH2OH / CH2CH2OH / **85**

G30 = NO2 / alkyl<(1-6)> / alkenyl<(2-6)> / alkynyl<(2-6)> / alkoxy<(1-)> / alkylamino<(1-6)> / alkyl<(1-6)> (SR alkoxy<(1-4)>) / alkyl<(1-6)> (SR alkylamino<(1-6)>) / CN / F / Cl / Br / I / CF3 / OH / CH2OH / CH2CH2OH / 87

G31 = alkyl<(1-6)> / alkenyl<(2-6)> / alkynyl<(2-6)> / alkoxy<(1-4)> / CHO / alkylcarbonyl<(1-4)> / alkylamino<(1-6)> / alkyl<(1-6)> (SR alkoxy<(1-4)>) / alkyl<(1-6)> (SR alkylamino<(1-6)>) / NO2 / CN / F / Cl / Br / I / CF3 / OH / CH2OH / CH2CH2OH / 89 / (SC Me)

C(O)-G32
89

G32 = OH / alkoxy<(1-6)> / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / Hy<EC (5-7) A (1-) N, AN (1) N>
G33 = O / S / 93-6 94-92

H2C—O
93 94

G34 = H / 4

G1—G2—G4—C(O)
4

MPL: claim 1
NTE: also incorporates claim 10
NTE: or pharmaceutically acceptable salts, or in vivo hydrolyzable derivatives
NTE: additional ring formation also claimed

L3 ANSWER 15 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:366693 MARPAT
TITLE: Preparation of bis(aminoalkyl- or amidinophenoxy)arylene- and heteroatom-interrupted alkanes and analogs as tryptase inhibitors
INVENTOR(S): Anderskewitz, Ralf; Braun, Christine; Hamm, Rainer; Disse, Bernd; Jennewein, Hans Michael; Speck, Georg
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 36 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

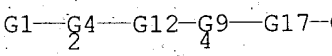
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19955476	A1	20010523	DE 1999-19955476	19991118
WO 2001036374	A2	20010525	WO 2000-EP11216	20001114
WO 2001036374	A3	20020411		
W: AE, AU, BG, BR, CA, CN, CZ, EE, HU, ID, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1250317	A2	20021023	EP 2000-987242	20001114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				

PRIORITY APPLN. INFO.: DE 1999-19955476 19991118
WO 2000-EP11216 20001114

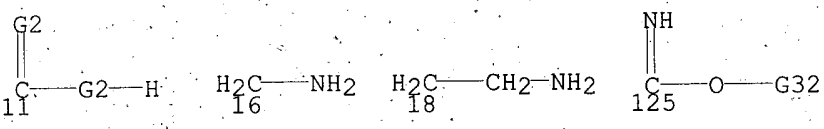
AB B1Z1X1Z2X2ZX3Z3X4Z4B2 [I; B1,B2 = C(:NR1)NHR1', CH2NH2, CH2CH2NH2, ureido; R1,R1' = OH, COR2, CO2R2; R2 = H, alkyl, aryl(alkyl); X1-X4 = bond, CH2, CH2CH2, CH2O, CH2NH, etc.; Z = (heteroatom-interrupted)alkylene, G1(CH2)rG2 [X2 or X3 = (CH2)1-2], E1(CH2)rE2, etc.; E1,E2 = azacycloalkylene; G1,G1 = bond or cycloalkylene; Z1-Z4 = (un)substituted (hetero)arylene; r = 0-6] were prepd. Thus, 3-(ClH2C)C6H4CH2OC6H4(CH2CH2NHBoc)-4 was condensed with (CH2CMe2NH2)2 to give, after deprotection, the N,N'-bisbenzylated hexandiamine.4HCl. Data

for biol. activity of I were given.

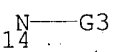
MSTR 1



G1 = 11 / 16 / 18 / NHC(NH)NH2 / 125 / CN



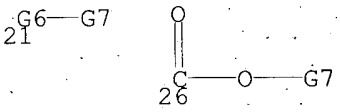
G2 = NH / 14



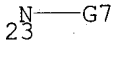
G3 = OH / CHO / alkylcarbonyl<(1-18)> / arylcarbonyl / alkylcarbonyl<(1-6)> (SR aryl) / CO2H / alkoxycarbonyl<(1-18)> / aryloxycarbonyl / alkoxycarbonyl<(1-6)> (SR aryl)

G4 = **aryl<(6-10)> (SO (1-4) G5)** / heteroaryl<EC (0-) N (0-) O (0-) S (0) OTHERQ, RA (5-10) A, RC (1-2)> (SO (1-4) G5) / (SC p-C6H4)

G5 = cycloalkyl<(3-10)> / F / Cl / Br / I / OH / SH / NH2 / 21 / **CO2H** / 26 / alkyl<(1-6)> (SO (1-) G8) / alkenyl<(2-6)> (SO (1-) G8) / alkynyl<(2-6)> (SO (1-) G8)



G6 = O / S / NH / 23



G7 = alkyl<(1-6)> (SO (1-) F) / cycloalkyl<(3-6)> (SO (1-) F)

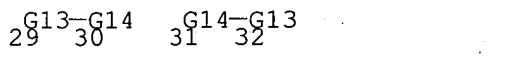
G8 = F / OH / alkoxy<(1-6)> (SO (1-) F) / cycloalkyloxy<(3-6)> (SO (1-) F)

G9 = **aryl<(6-10)> (SO (1-4) G5)** / heteroaryl<EC (0-) N (0-) O (0-) S (0) OTHERQ, RA (5-10) A, RC (1-2)> (SO (1-4) G5) / (SC phenylene)

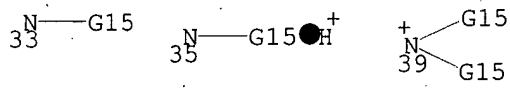
G10 = aryl<(6-10)> (SO (1-4) G5) / heteroaryl<EC (0-) N (0-) O (0-) S (0) OTHERQ, RA (5-10) A, RC (1-2)> (SO (1-4) G5) / (SC phenylene)

G11 = aryl<(6-10)> (SO (1-4) G5) / heteroaryl<EC (0-) N (0-) O (0-) S (0) OTHERQ, RA (5-10) A, RC (1-2)> (SO (1-4) G5) / (SC p-C6H4)

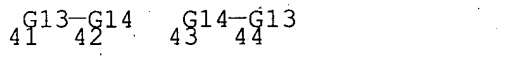
G12 = G13 / 29-2 30-4 / 31-2 32-4



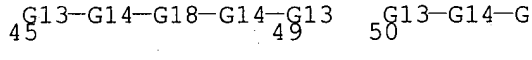
G13 = **(1-2) CH2**
G14 = O / S / NH / 33 / 35 / 39

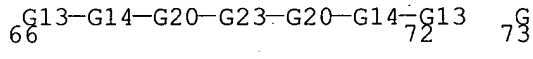


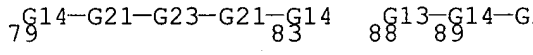
G15 = alkyl<(1-6)> (SO (1-) F) /
cycloalkyl<(3-6)> (SO (1-) F) / (SC Me / cyclopropyl / Bu-n)
G16 = G13 / 41-6 42-8 / 43-6 44-8

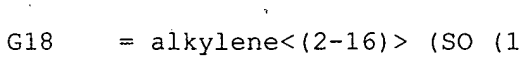


G17 = 45-4 49-6 / 50-4 54-6 / 55-4 59-6 / 66-4 72-6 /
73-4 78-6 / 79-4 83-6 / 88-4 92-6 / 93-4 96-6 / 97-4 99-6

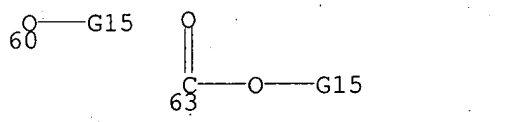








G18 = alkylene<(2-16)> (SO (1-) G19) /
alkenylene<(2-16)> (SO (1-) G19) / alkynylene<(2-16)>
G19 = F / alkyl<(1-6)> (SO (1-) F) /
cycloalkyl<(3-6)> (SO (1-) F) / OH / 60 / CO2H / 63



G20 = G22 / alkylene<(2-4)> (SR (1-2) alkyl<(1-6)>)
G21 = alkylene<(3-5)> (SR (1-2) alkyl<(1-6)>)
G22 = (2-4) CH2
G23 = arylene (SO (1-) G24) /
cycloalkylene<(3-10)> (SO (1-) G24) / O / S / NH / 86

G24 = F / alkyl<(1-6)> (SO (1-) F) /
cycloalkyl<(3-6)> (SO (1-) F) / OH / 84

O——G15
84

G25 = NULL / G26 / 100-89 101-91 / 102-89 103-91 /
104-89 106-91 / cycloalkylene<(3-10)> /
Hy<EC (1-2) N (0) OTHERQ (1-9) C, AN (1-) N, AR (0),
BD (ALL) SE, RC (1), RS (1) M3 (1) X10>

G27—G26 G26—G27 G27—G26—G27
100 101 102 103 104 106

G26 = (1-6) CH2
G27 = cycloalkylene<(3-10)> /
Hy<EC (1-2) N (0) OTHERQ (1-9) C, AN (1-) N, AR (0),
BD (ALL) SE, RC (1), RS (1) M3 (1) X10>
G28 = G29 / 107-94 108-96 / 109-94 111-96 / 112-94 115-96

G27—G29 G26—G27—G13 G27—G26—G27—G13
107 108 109 111 112 115

G29 = (1-8) CH2
G30 = G31 / 116-97 118-99 / 119-97 123-99

G13—G27—G31 G13—G27—G26—G27—G13
116 118 119 123

G31 = (2-10) CH2
G32 = alkyl<(1-6)>
MPL: claim 1
NTE: also incorporates claims 10 and 11
NTE: and tautomers and pharmacologically acceptable acid addition salts
NTE: substitution is restricted
STE: and racemates, enantiomers, diastereomers, and their mixtures

MSTR 2

G1—G4—G12—G9—G17
2 4

G1 = 11 / 16 / 18 / NHC(NH)NH2

G2
‖
C——G2—H H_2C——NH_2 H_2C——CH_2—NH_2
11 16 18

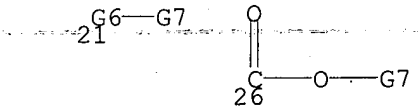
G2 = NH / 14

N——G3
14

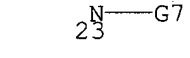
G3 = OH / CHO / alkylcarbonyl<(1-18)> / arylcarbonyl / alkylcarbonyl<(1-6)> (SR aryl) / CO2H / alkoxycarbonyl<(1-18)> / aryloxycarbonyl / alkoxycarbonyl<(1-6)> (SR aryl)

G4 = **aryl<(6-10)> (SO (1-4) G5)** / heteroaryl<EC (0-) N (0-) O (0-) S (0) OTHERQ, RA (5-10) A, RC (1-2)> (SO (1-4) G5) / (SC p-C6H4)

G5 = cycloalkyl<(3-10)> / F / Cl / Br / I / OH / SH / NH2 / 21 / **CO2H** / 26 / alkyl<(1-6)> (SO (1-) G8) / alkenyl<(2-6)> (SO (1-) G8) / alkynyl<(2-6)> (SO (1-) G8)



G6 = O / S / NH / 23

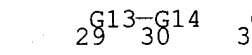


G7 = alkyl<(1-6)> (SO (1-) F) / cycloalkyl<(3-6)> (SO (1-) F)

G8 = F / OH / alkoxy<(1-6)> (SO (1-) F) / cycloalkyloxy<(3-6)> (SO (1-) F)

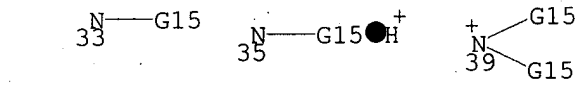
G9 = **aryl<(6-10)> (SO (1-4) G5)** / heteroaryl<EC (0-) N (0-) O (0-) S (0) OTHERQ, RA (5-10) A, RC (1-2)> (SO (1-4) G5) / (SC phenylene)

G12 = G13 / 29-2 30-4 / 31-2 32-4



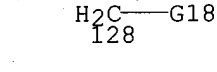
G13 = **(1-2) CH2**

G14 = **O** / S / NH / 33 / 35 / 39



G15 = alkyl<(1-6)> (SO (1-) F) / cycloalkyl<(3-6)> (SO (1-) F) / (SC Me / cyclopropyl / Bu-n)

G17 = CHO / 128



G18 = F / Cl / Br / I / 130

G19 = alkyl / aryl

DER: as protected derivatives

MPL: claim 13

NTE: also incorporates claim 14

L3 ANSWER 16 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:100762 MARPAT
TITLE: Preparation of pyridine derivatives and medicinal use thereof
INVENTOR(S): Iino, Yukio; Fujita, Kohichi; Kodaira, Ariko; Hatanaka, Toshihiro; Takehana, Kenji; Kobayashi, Tsuyoshi; Konishi, Atsushi; Yamamoto, Takashi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002359	A1	20010111	WO 2000-JP4298	20000629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1193255	A1	20020403	EP 2000-940879	20000629
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BR 2000012046	A	20020514	BR 2000-12046	20000629
US 2002133005	A1	20020919	US 2001-29871	20011231
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			JP 2000-71706	20000315
			WO 2000-JP4298	20000629

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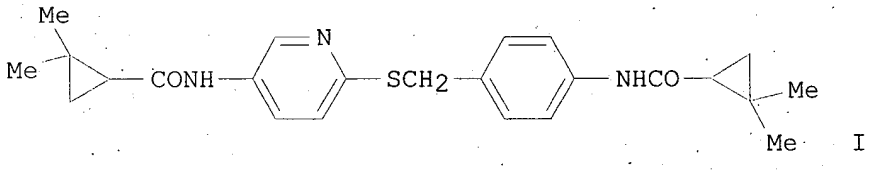


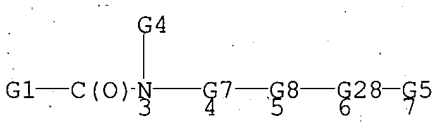
I

AB Heterocyclic compds. represented by the following general formula R1-CO-N(R2)-A-X-B-N(R3)-Y-(CH2)n-R4 [R1 = (un)substituted or cycloalkenyl; R2, R3 = H, alkyl; R4 = (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, or heterocyclyl having .gtoreq.1 heteroatom(s); A = (un)substituted heterocyclic ring; B = (un)substituted arom. or heterocyclic ring; n = 0-6; Y = a bond between atoms, CO, CO2, CONR5, C(S)NR5, SO, SO2 (wherein R5 = H, alkyl); X = a bond between atoms, O, OCHR7, CHR8O, O2C, CO2, OC(S), C(S)O, S, SO, SO2, SCHR9, CHR10S, SC(O), C(O)S, SC(S), C(S)S, SO2 NR11, NR12SO2, NR13, etc.; R7 - R10 = H, alkyl; R11 - R13 = H, alkyl, acyl] or pharmacol. acceptable salts thereof are prepd. These compds. have inhibitory effects on AP-1 activity, NF-kappa B activity, inflammatory cytokine prodn., matrix metalloprotease prodn., expression of inflammatory cell adhesion factor, etc. and are usable as drugs such as antiinflammatory, antirheumatic, antiviral agents,

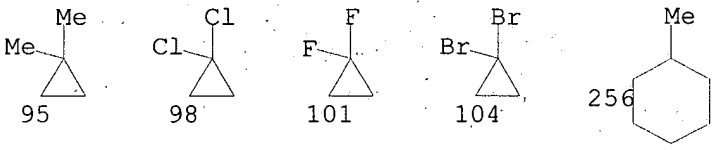
immunosuppressants, cancer metastasis inhibitors, and antiarteriosclerotics. Thus, 2-mercapto-5-nitropyridine was treated with NaH in DMF and then alkylated by 1-bromomethyl-4-nitrobenzene at room temp. for 1.5 h to give 2-(4-nitrobenzylthio)-5-nitropyridine which was reduced by Zn/AcOH in THF at room temp. for 16 h to 2-(4-aminobenzylthio)-5-aminopyridine and then acylated by 2,2-dimethylcyclopropanecarbonyl chloride in the presence of Et3N in CH2Cl2 at room temp. for 17 h to give 2-(4-(2,2-dimethylcyclopropanecarbonylamino)benzylthio)-5-(2,2-dimethylcyclopropanecarbonylamino)pyridine (I). I in vitro inhibited NF-kappa B activity with IC50 of 0.015 .mu.g/mL in an assay measuring .beta.-galactosidase activity expressed in HUVEC cells and driven by NF-kappa B-binding sequence-fused SV40 T antigen min. promoter.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1



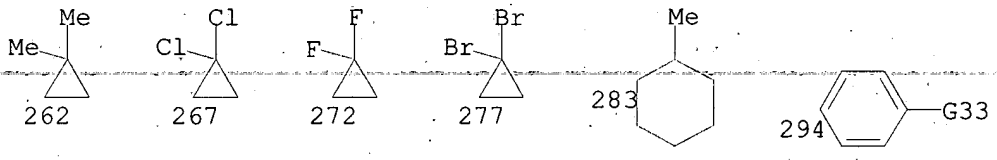
G1 = cycloalkyl<(3-6)> (SO (1-) G2) / cycloalkenyl<(3-6)> (SO (1-) G2) / (SC cyclopropyl (SO) / 95 / 98 / 101 / 104 / 256)



G2 = R / (EX F / Cl / Br / I / alkyl<(1-6)> (SO) / CO2H / alkoxycarbonyl / CN / alkylamino<(1-6)> / dialkylamino<(1-6)> / NH2 (SR))

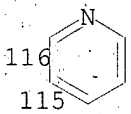
G4 = H / alkyl<(1-6)>

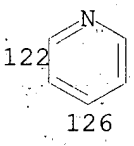
G5 = alkyl<(1-6)> (SO (1-) G6) / alkenyl<(2-6)> (SO) / cycloalkyl<(3-6)> (SO (1-) G2) / cycloalkenyl<(3-6)> (SO (1-) G2) / aryl (SO (1-3) G2) / heteroaryl (SO (1-3) G2) / (SC 262 / 267 / 272 / 277 / 283 / 294)

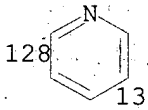


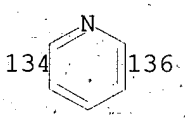
G6 = R / (EX F / Cl / Br / I / OH / alkoxy<(1-6)> / cycloalkyloxy<(3-6)> / CO2H / alkoxycarbonyl / CN / alkylamino<(1-6)> / dialkylamino<(1-6)> / NH2 (SR))

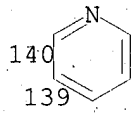
G7 = **Hy<EC (0-) N (0-) O (0-) S, RC (1-2), RS (0-) E5 (0-) E6 (0-) E7 (0) OTHER> (SO (1-3) G27)** / (SC 116-3 115-5 / 122-3 126-5 / 128-3 131-5 / 134-3 136-5 / 139-3 140-5 / 145-3 150-5 / 151-3 155-5 / 157-3 160-5 / 168-3 164-5 / 174-3 169-5 / 182-3 181-5 / 188-3 186-5 / 194-3 191-5 / 199-3 200-5 / 205-3 204-5 / 211-3 209-5 / 218-3 217-5 / 224-3 222-5 / 230-3 226-5 / 235-3 236-5 / 241-3 238-5 / 244-3 248-5 / 250-3 253-5)

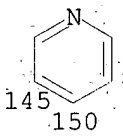


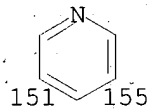


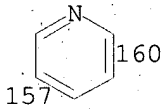


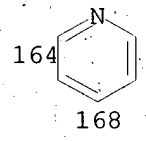


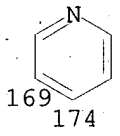


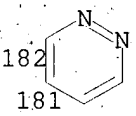


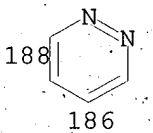


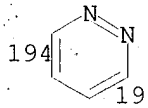


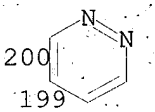


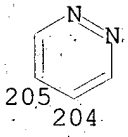


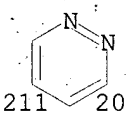


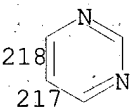


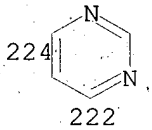


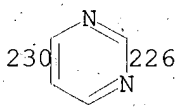


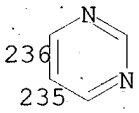


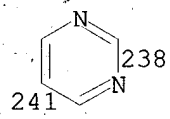


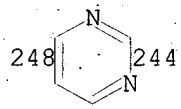


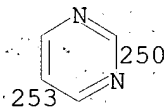




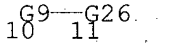




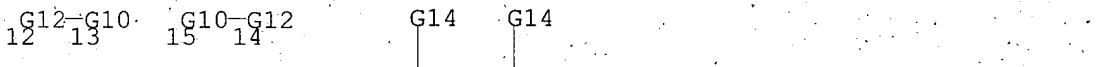


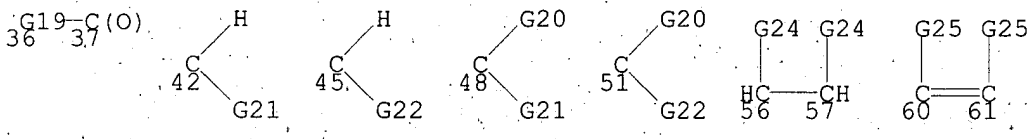


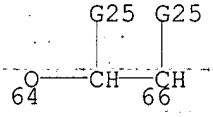
G8 = arylene<RC (1-2)> (SO (1-) G27) /
Hy<EC (0-) N (0-) O (0-) S, RC (1-2),
RS (0-) E5 (0-) E6 (0-) E7 (0) OTHER> (SO (1-3) G27) /
10-4 11-6 / (SC phenylene (SO))



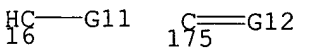
G9 = O / 12-4 13-11 / 15-4 14-11 / S / S(O) / SO2 /
18-4 19-11 / 20-4 21-11 / 24 / 28 / 34-4 35-11 / 36-4 37-11 /
42 / 45 / 48 / 51 / 56-4 57-11 / 60-4 61-11 / 64-4 66-11



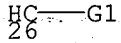




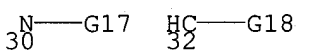
G10 = **16** / 175



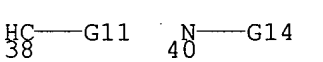
G11 = H / alkyl<(1-6)>
G12 = **O** / S
G14 = H / alkyl<(1-6)> / acyl
G15 = SO2 / 26



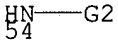
G16 = O / 30 / 32



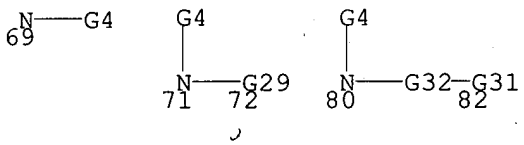
G17 = OH / alkoxy<(1-6)> / acyloxy
G18 = H / alkyl<(1-6)> / acyl
G19 = 38 / 40



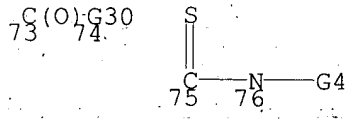
G20 = alkyl<(1-6)>
G21 = H / OH / SH / alkoxy<(1-6)> / cycloalkyloxy<(3-6)> / alkylthio<(1-6)> / cycloalkylthio<(3-6)> / acyloxy / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / 54



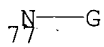
G22 = alkyl<(1-6)> (SO (1-) G6) / CO2H / alkoxycarbonyl / CONH2 / CN
G23 = R<TX "protecting group">
G24 = H / OH / alkyl<(1-6)>
G25 = H / alkyl<(1-6)>
G26 = arylene<RC (1-2)> (SO (1-) G27) / **Hy<EC (0-) N (0-) O (0-) S, RC (1-2), RS (0-) E5 (0-) E6 (0-) E7 (0) OTHER> (SO (1-3) G27)** / (SC phenylene (SO))
G27 = R / (EX F / Cl / Br / I / alkyl<(1-6)> (SO) / OH / alkoxy<(1-6)> / cycloalkyloxy<(3-6)> / **CO2H** / alkoxycarbonyl / CN / alkylamino<(1-6)> / dialkylamino<(1-6)> / NH2 (SR))
G28 = 69 / 71-5 72-7 / 80-5 82-7



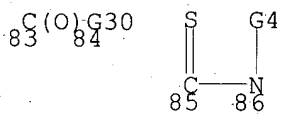
G29 = C(O) / 73-71 74-7 / 75-71 76-7 / S(O) / SO2 / alkylene<EC (1-6) C, DC (0) M3>



G30 = O / 77



G31 = alkylene<EC (1-6) C, DC (0) M3>
G32 = C(O) / 83-80 84-82 / 85-80 86-82 / S(O) / SO2

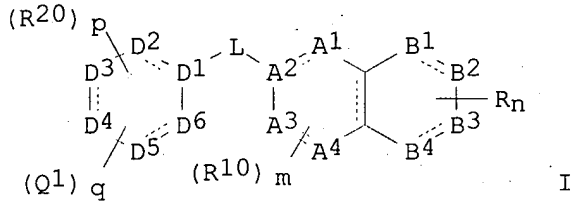


G33 = H / Cl / OMe
MPL: claim 1
NTE: pharmaceutically acceptable salts

L3 ANSWER 17 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:309849 MARPAT
TITLE: Preparation of arylcarboxamidines as glycoprotein IIb/IIIa antagonists.
INVENTOR(S): Fisher, Matthew J.; Happ, Anne Marie; Jakubowski, Joseph A.; Kinnick, Michael Dean; Kline, Allen D.; Morin, John Michael, Jr.; Sall, Daniel J.; Skelton, Marshall A.; Vasileff, Robert Theodore
PATENT ASSIGNEE(S): Eli Lilly & Co., USA
SOURCE: U.S., 69 pp., Cont.-in-part of U.S. 5,618,843.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6137002	A	20001024	US 1996-710823	19960923
US 5618843	A	19970408	US 1994-255821	19940708
US 6472405	B1	20021029	US 1999-299404	19990426
PRIORITY APPLN. INFO.:			US 1993-96220	19930722
			US 1994-255821	19940708
			US 1996-710823	19960923

GI



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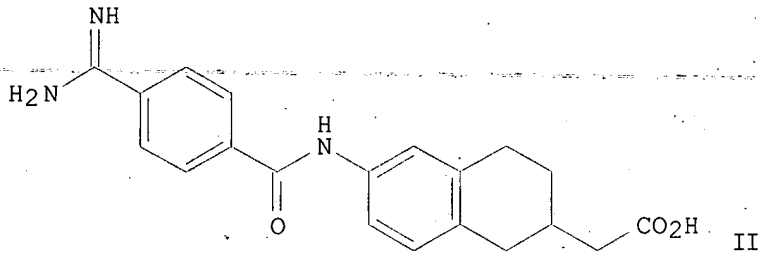
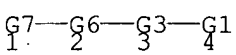


II

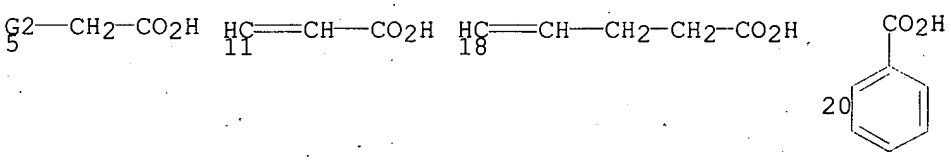
AB Title compds. [I; rings AB = naphthyl, dihydronaphthyl, tetralinyl, decalinyl; R = H, alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, OH, CO2H, amino, etc.; m, n = 2-6; p = 0-8; q = 1-3; R3 = CH2CO2H, NHCH2CO2H, OCH2CO2H, CH2CH2CO2H, CH:CHCO2H, CO2H, etc.; R10 = H, alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, aryl, OH, alkoxy, aralkoxy, acyl, cyano, halo, NO2, etc.; L = 1-4 membered linking group contg. C, N, S, or O atoms; D = 6-membered ring wherein D1-D6 = C, N, O, S; .gtoreq.2 of D1-D6 = C; Q1 = (substituted) amino, imino, amidino, aminomethyleneamino, iminomethylamino, alkylamino, pyrrolyl, imidazolyl, pyranyl, pyrimidinyl, phthalazinyl, phenanthrolinyl, etc.; R20 = H, alkyl, haloalkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, OH, alkoxy, (substituted) amino, etc.], were prepd. Thus, title compd. (II) (prepd. from 6-benzyloxycarbonylamino-1-tetralone) inhibited ADP-induced platelet aggregation with IC50 = 0.19 .mu.M.

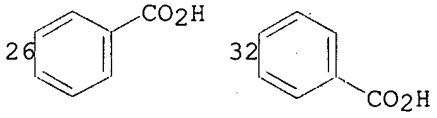
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1

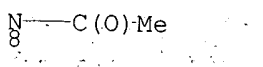


G1 = R<TX "acidic group"> / CH2CO2H / 5 / CH2CH2CO2H / 11 / 18 / 20 / 26 / 32 / CO2H

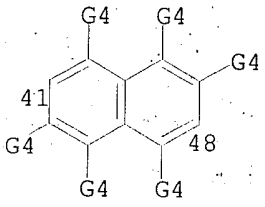


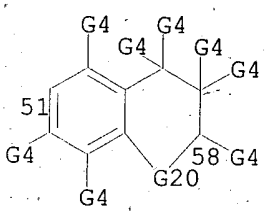


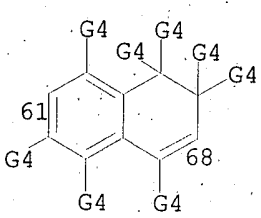
G2 = NH / O / 8

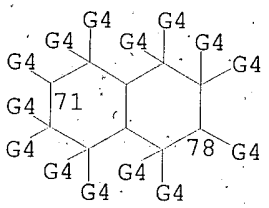


G3 = 41-2 48-4 / 51-2 58-4 / 61-2 68-4 / 71-2 78-4 /
Hy<EC (10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ (6-) C, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G21) /
Cb<EC (10) C, FA (2) C, RC (2), RS (2) E6 (0) OTHER>
(SO (1-) G21) / 207







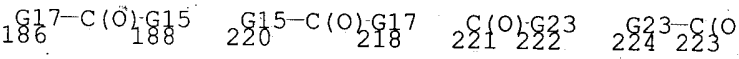


G22=G17
207

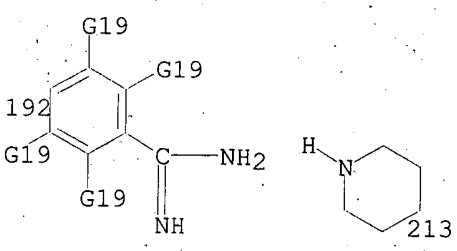
G4 = H / alkyl<(1-10)> (SO (1-3) G5) / alkenyl<(2-10)> /
alkynyl<(2-10)> / cycloalkyl / aryl /
alkyl<(1-10)> (SR (1-3) aryl) / OH /
alkoxy<(1-10)> (SO (1-3) aryl) / NH2 (SO) / CONH2 / CO2H /
acyl / CN / F / Cl / Br / I / NO2 / SO3H

G5 = F / Cl / Br / I

G6 = R<TX "linking group",
EC (0-) C (0-) O (0-) S (0-) N>/ NULL / (SC 186-1 188-3 /
220-1 218-3) / (EX 221-1 222-3 / 224-1 223-3 / ethynylene /
CH=CH / CH2CH2 / **225-1 226-3** / 228-1 227-3)



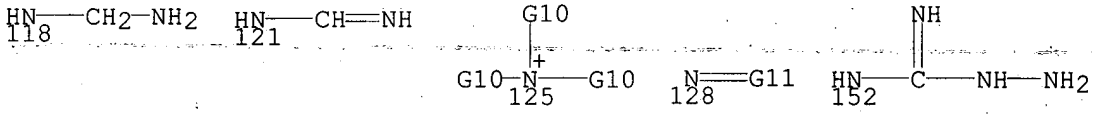
G7 = **Cb<EC (6) C, RC (1), RS (1) E6> (SR (1-) G8)** /
Hy<EC (6) A (0-) O (0-) S (0-) N (0) OTHERQ (2-) C, RC (1),
RS (1) E6> (SR (1-) G8) / R<TX "basic group"> / (SC 192) /
(EX 213)

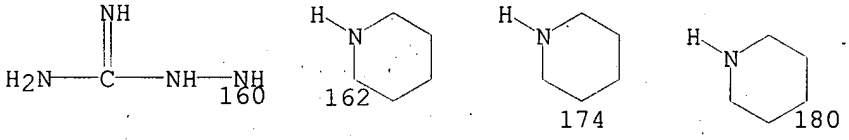


G8 = (1-3) G9 / alkyl<(1-10)> (SO (1-3) G5) /
alkenyl<(2-10)> / alkynyl<(2-10)> / cycloalkyl / aryl /

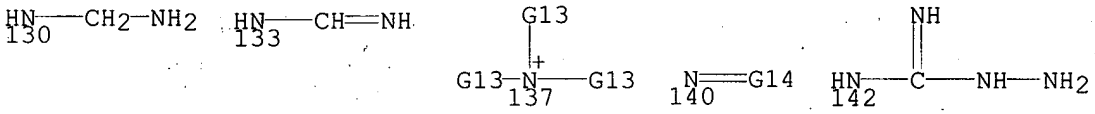
alkyl<(1-10)> (SR (1-3) aryl) / OH /
alkoxy<(1-10)> (SO (1-3) aryl) / NH2 (SO) / CONH2 / **CO2H** /
acyl / CN / F / Cl / Br / I / NO2 / SO3H

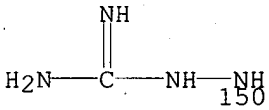
G9 = R<TX "organic group"> / NH2 / C(NH)NH2 / 118 / 121 /
152 / NHC(NH)NH2 / 160 / alkylamino<(1-10)> (SO) /
dialkylamino<(1-10)> (SO) / 125 / 128 /
Hy<EC (6) A (1) Q (1) O (0) OTHERQ, RC (1), RS (1) E6> (SO) /
Hy<EC (5-14) A (1-4) Q (1-4) N (0-1) S (0-1) O (0-1) As (0)
OTHERQ, RC (1-3), RS (0-) E5 (0-) E6 (0) OTHER> (SO G12) /
(SC piperidino / 162 / 174 / 180)



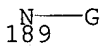


G10 = alkyl<(1-10)> (SO)
G11 = alkylidene<(1-10)> (SO)
G12 = NH2 / C(NH)NH2 / 130 / 133 / NHC(NH)NH2 / 142 /
150 / alkylamino<(1-10)> / dialkylamino<(1-10)> / 137 / 140

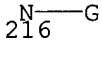




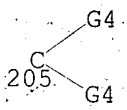
G13 = alkyl<(1-10)>
G14 = alkylidene<(1-10)>
G15 = NH / 189



G17 = O / S / NH / 216



G18 = alkyl<(1-10)>
G19 = H / R
G20 = 205 / C(O)



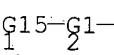
G21 = alkyl<(1-10)> (SO (1-3) G5) / alkenyl<(2-10)> /
alkynyl<(2-10)> / cycloalkyl / aryl /
alkyl<(1-10)> (SR (1-3) aryl) / OH /
alkoxy<(1-10)> (SO (1-3) aryl) / NH2 (SO) / CONH2 / **CO2H** /
acyl / CN / F / Cl / Br / I / NO2 / SO3H
G22 = Hy<EC (10) A (1-4) Q (0-) N (0-) O (0-) S (0)
OTHERQ (6-) C, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO) /
Cb<EC (10) C, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO)
G23 = O / NH
MPL: claim 1
NTE: also incorporates broader disclosure
NTE: additional oxo and thioxo formation also claimed
NTE: or pharmaceutically acceptable salts, solvates or prodrug derivatives

L3 ANSWER 18 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:222437 MARPAT
TITLE: Method for the radical alkylation of arenes
INVENTOR(S): Murphy, John; Graham, Stephen
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

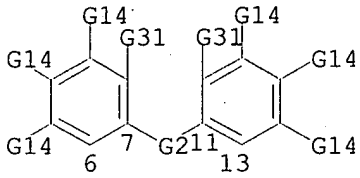
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 987235	A1	20000322	EP 1999-116091	19990817
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			EP 1998-115971	19980825

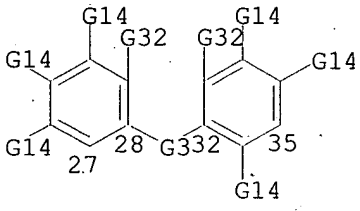
OTHER SOURCE(S): CASREACT 132:222437
AB The title process comprises a method for the conversion of alkenes or arenes with iodoalkenes, aryl iodides or arenediazonium salts in the presence of hypophosphorous acid or its derivs. and a radical initiator. Thus, O-allyl-3,5-diiodosalicylic acid was refluxed with H3PO2/AIBN/H2O to give 3-methyl-2,3-dihydrobezofuran-7-carboxylic acid.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

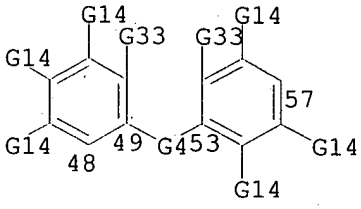
MSTR 3

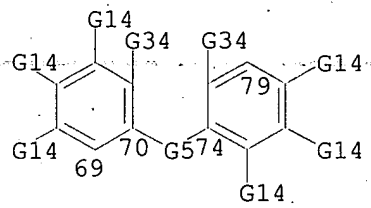


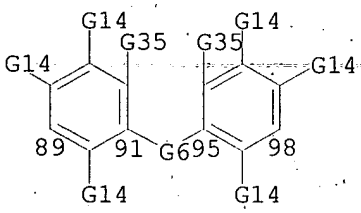
G1 = 6-1 13-3 / 27-1 35-3 / 48-1 57-3 / 69-1 79-3 /
89-1 98-3 / 110-1 120-3 / 131-1 142-3 / 151-1 162-3 /
172-1 184-3 / 198-1 205-3

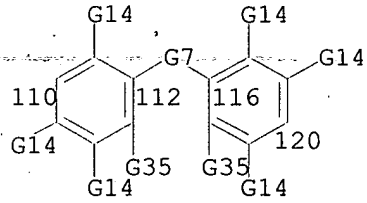


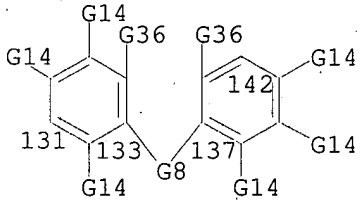


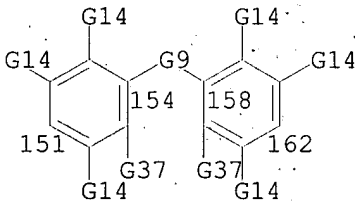


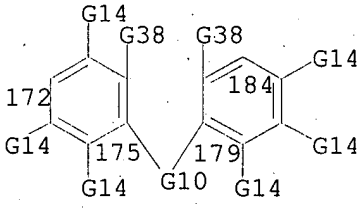


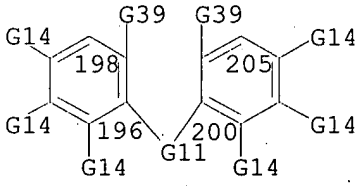




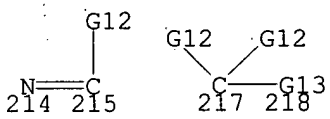




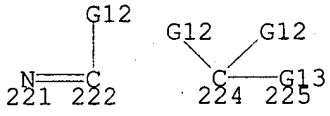




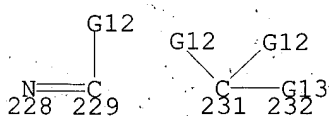
G2 = O / S / NH (SO) / 214-7 215-11 / CH2 (SO) / CH=CH (SO) / CH2CH2 (SO) / 217-7 218-11



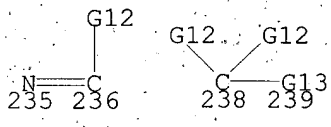
G3 = O / S / NH (SO) / 221-28 222-32 / CH2 (SO) / CH=CH (SO) / CH2CH2 (SO) / 224-28 225-32



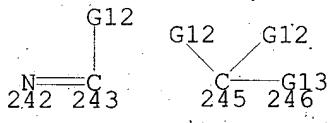
G4 = O / S / NH (SO) / 228-49 229-53 / CH2 (SO) / CH=CH (SO) / CH2CH2 (SO) / 231-49 232-53



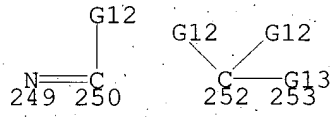
G5 = O / S / NH (SO) / 235-70 236-74 / CH2 (SO) /
CH=CH (SO) / CH2CH2 (SO) / 238-70 239-74



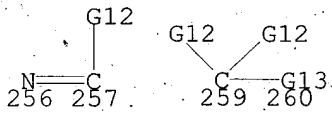
G6 = O / S / NH (SO) / 242-91 243-95 / CH2 (SO) /
CH=CH (SO) / CH2CH2 (SO) / **245-91 246-95**



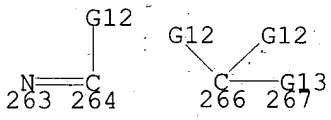
G7 = O / S / NH (SO) / 249-112 250-116 / CH2 (SO) /
CH=CH (SO) / CH2CH2 (SO) / 252-112 253-116



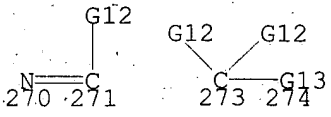
G8 = O / S / NH (SO) / 256-133 257-137 / CH2 (SO) /
CH=CH (SO) / CH2CH2 (SO) / 259-133 260-137



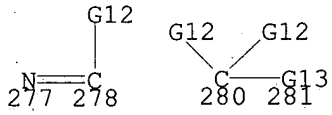
G9 = O / S / NH (SO) / 263-154 264-158 / CH2 (SO) /
CH=CH (SO) / CH2CH2 (SO) / 266-154 267-158



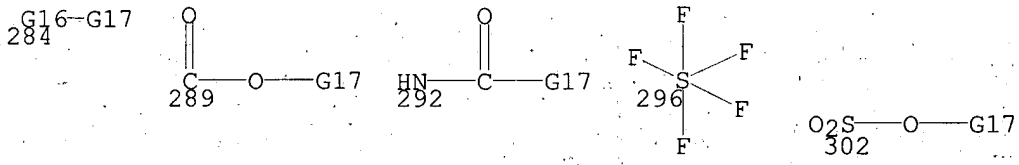
G10 = O / S / NH (SO) / 270-175 271-179 / CH2 (SO) /
CH=CH (SO) / CH2CH2 (SO) / 273-175 274-179

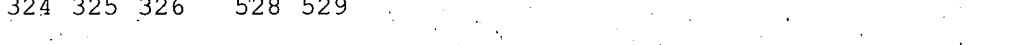


G11 = O / S / NH (SO) / 277-196 278-200 / CH2 (SO) /
CH=CH (SO) / CH2CH2 (SO) / 280-196 281-200

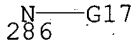


G12 = H / R
G13 = **O** / NH (SO)
G14 = H / R
G15 = H / F / Br / Cl / CN / NO2 / NH2 / OH / SH / 284 / **CO2H** / 289 / NHCHO / 292 / 296 / SO3H / 302 / alkyl<(1-12)> (SO (1-) G19) / R<TX "mesogenic group"> / (SC 324 / 528)

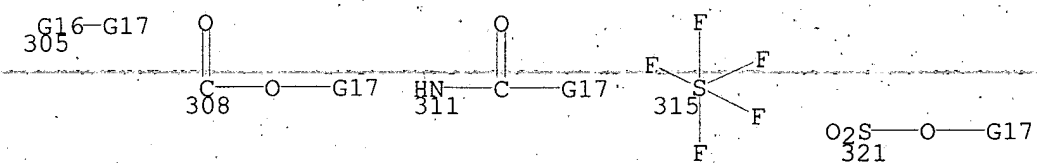




G16 = NH / 286 / O / S



G17 = alkyl<(1-12)> / alkoxy<(1-12)> / Ph (SO (1-) G18) / Hy<EC (1-2) N (4-5) C (0) OTHERQ, AN (0) N, AR (1-), BD (ALL) N, RC (1), RS (1) E6> (SO (1-) G18)
G18 = F / Cl / Br / CF3 / CN / NO2 / alkyl<(1-12)> / alkoxy<(1-12)>
G19 = F / Br / Cl / CF3 / CN
G20 = H / F / Br / Cl / CN / NO2 / NH2 / OH / SH / 305 / **CO2H** / 308 / NHCHO / 311 / 315 / SO3H / 321 / alkyl<(1-12)> (SO (1-) G19) / R<TX "mesogenic group"> / (SC 327 / 530)



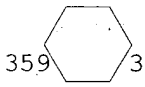
G21 = CH2CH2 / ethynylene / 330-2 331-325 / 332-2 333-325 / 334-2 335-325 / 336-2 337-325 / 338-2 339-325 / 340-2 341-325

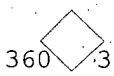
G22—O O—G22 HC=N N=CH H2C—S S—CH2
330 331 332 333 334 335 336 337 338 339 340 341

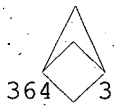
G22 = C(O) / CH2
G23 = CH2CH2 / ethynylene / 342-2 343-328 /
344-2 345-328 / 346-2 347-328 / 348-2 349-328 /
350-2 351-328 / 352-2 353-328

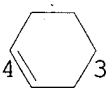
G22—O O—G22 HC=N N=CH H2C—S S—CH2
342 343 344 345 346 347 348 349 350 351 352 353

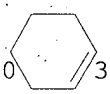
G24 = 359-324 356-326 / Hy<EC (1-2) Q (0-) O (0-) S (0)
OTHERQ (4-5) C, AN (2-) C, AR (0), BD (ALL) SE, RC (1),
RS (1) E6> / p-C6H4 (SO (1-) G28) /
Hy<EC (1-2) N (4-5) C (0) OTHERQ, AN (2-) C (0) N, AR (1-),
BD (ALL) N, RC (1), RS (1) E6> / 360-324 362-326 /
364-324 366-326 / 374-324 371-326 / 380-324 377-326 /
386-324 383-326 / 394-324 391-326 / 400-324 397-326 /
Cb<EC (10) C, AN (2) C, AR (0), BD (ALL) SE, RC (2),
RS (2) E6 (0) OTHER> / Cb<EC (10) C, AN (2) C, AR (1-),
BD (6-) N, RC (2), RS (2) E6 (0) OTHER> /
(EX 671-324 668-326 / 677-324 674-326)

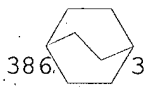


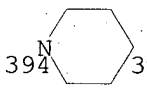


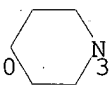


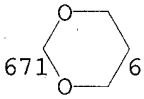


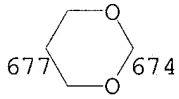












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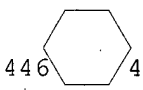
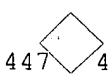
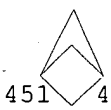
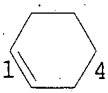
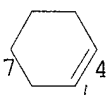
OTHERQ (4-5) C, AN (2-) C, AR (0), BD (ALL) SE, RC (1),
RS (1) E6> / p-C6H4 (SO (1-) G28) /
Hy<EC (1-2) N (4-5) C (0) OTHERQ, AN (2-) C (0) N, AR (1-),
BD (ALL) N, RC (1), RS (1) E6> / 447-327 449-329 /
451-327 453-329 / 461-327 458-329 / 467-327 464-329 /
473-327 470-329 / 481-327 478-329 / 487-327 484-329 /
Cb<EC (10) C, AN (2) C, AR (0), BD (ALL) SE, RC (2),
RS (2) E6 (0) OTHER> / Cb<EC (10) C, AN (2) C, AR (1-),
BD (6-) N, RC (2), RS (2) E6 (0) OTHER> /
(EX 683-327 680-329 / 689-327 686-329)

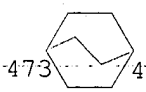


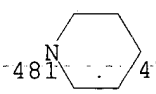


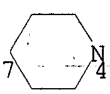


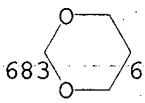


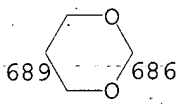




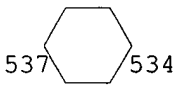


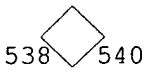


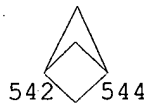


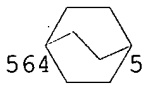


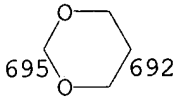
G26 = 537-2 534-529 / Hy<EC (1-2) Q (0-) O (0-) S (0)
OTHERQ (4-5) C, AN (2-) C, AR (0), BD (ALL) SE, RC (1),
RS (1) E6> / p-C6H4 (SO (1-) G28) /
Hy<EC (1-2) N (4-5) C (0) OTHERQ, AN (2-) C (0) N, AR (1-),
BD (ALL) N, RC (1), RS (1) E6> / 538-2 540-529 /
542-2 544-529 / Cb<EC (6) C, AN (2) C, AR (0), BD (1) DE,
RC (1), RS (1) E6> / 564-2 561-529 /
Hy<EC (1) N (5) C (0) OTHERQ, AN (1) N (1) C, AR (0),
BD (ALL) SE, RC (1), RS (1) E6> /
Cb<EC (10) C, AN (2) C, AR (0), BD (ALL) SE, RC (2),
RS (2) E6 (0) OTHER> / Cb<EC (10) C, AN (2) C, AR (1-),
BD (6-) N, RC (2), RS (2) E6 (0) OTHER> / (EX 695-2 692-529 /
701-2 698-529)

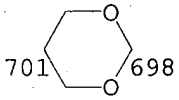




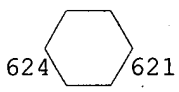


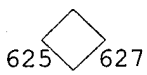


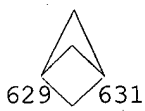


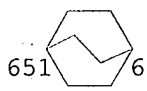


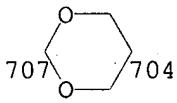
G27 = 624-2 621-531 / Hy<EC (1-2) Q (0-) O (0-) S (0)
OTHERQ (4-5) C, AN (2-) C, AR (0), BD (ALL) SE, RC (1),
RS (1) E6> / p-C6H4 (SO (1-) G28) /
Hy<EC (1-2) N (4-5) C (0) OTHERQ, AN (2-) C (0) N, AR (1-),
BD (ALL) N, RC (1), RS (1) E6> / 625-2 627-531 /
629-2 631-531 / Cb<EC (6) C, AN (2) C, AR (0), BD (1) DE,
RC (1), RS (1) E6> / 651-2 648-531 /
Hy<EC (1) N (5) C (0) OTHERQ, AN (1) N (1) C, AR (0),
BD (ALL) SE, RC (1), RS (1) E6> /
Cb<EC (10) C, AN (2) C, AR (0), BD (ALL) SE, RC (2),
RS (2) E6 (0) OTHER> / Cb<EC (10) C, AN (2) C, AR (1-),
BD (6-) N, RC (2), RS (2) E6 (0) OTHER> / (EX 707-2 704-531 /
713-2 710-531)

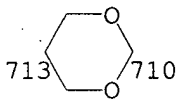




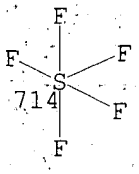








G28 = CN / F / Cl / Br
G29 = H / F / Cl / Br / Cl / CN / NO2 / 714 /
alkyl<(1-12)> (SO (1-) G30)



G30 = F / Cl / Br / CF3 / CN
G31 = (1) H / I / diazonium
G32 = (1) H / I / diazonium
G33 = (1) H / I / diazonium
G34 = (1) H / I / diazonium
G35 = (1) H / I / diazonium
G36 = (1) H / I / diazonium
G37 = (1) H / I / diazonium
G38 = (1) H / I / diazonium
G39 = (1) H / I / diazonium
MPL: claim 3
NTE: additional interruptions also claimed for alkyl groups in G15, G20, and G29
STE: all cyclohexylene rings are trans

L3 ANSWER 19 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:166133 MARPAT
TITLE: Preparation of hydroxy pipecolate hydroxamic acid derivatives as MMP inhibitors
INVENTOR(S): McClure, Kim Francis; Noe, Mark Carl; Letavic, Michael Anthony; Chupak, Louis Stanley
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000009485	A1	20000224	WO 1999-IB1388	19990805
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 9949247	A1	20000306	AU 1999-49247	19990805
BR 9912909	A	20010508	BR 1999-12909	19990805
EP 1104403	A1	20010606	EP 1999-933076	19990805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6329397	B1	20011211	US 1999-372946	19990812
NO 2001000686	A	20010409	NO 2001-686	20010209
US 2003008901	A1	20030109	US 2001-8943	20011203
PRIORITY APPLN. INFO.:			US 1998-96232P	19980812
			WO 1999-IB1388	19990805
			US 1999-372946	19990812

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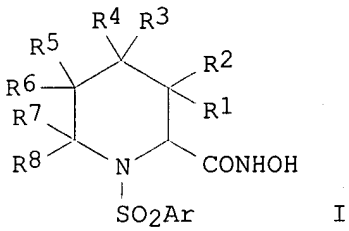
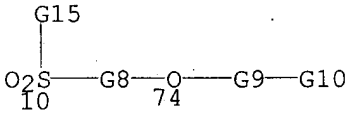


I

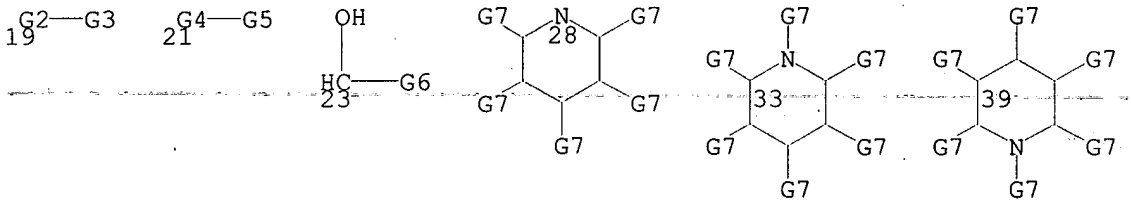
AB The title compds. I [R1 - R8 = H, OH, halogen, CN, (un)substituted (C1-6)alkyl, (un)substituted (C2-6)alkenyl, (un)substituted (C2-10)aryl, (un)substituted (C2-9)heteroaryl, etc; or R1 and R2, or R3 and R4, or R5 and R6 together = carbonyl or form a (C3-6)cycloalkyl, oxacyclohexyl, thiocyclohexyl, indanyl or tetralinyl ring; Ar = (un)substituted (C2-10)aryl, (un)substituted (C1-6)alkoxy, (un)substituted (C6-10)aryl, (un)substituted (C2-9)heteroaryl, etc] are prepd. Compds. of this invention had IC50 of less than 1 .mu.M in at least one of the assays for inhibiting activities against MMP-1, MMP-2, MMP-3, and MMP-13.

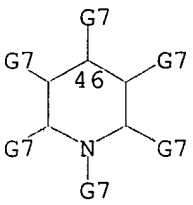
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1

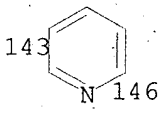


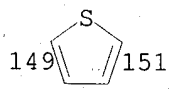
G1 = (1-) OH / H / X / CN / alkyl<(1-6)> (SO) / alkenyl<(2-6)> / 19 / alkynyl<(2-6)> / 21 / perfluoroalkyl<(1-6)> / aryl<(6-10)> (SO) / heteroaryl<(2-9)> (SO) / cycloalkyl<(3-6)> / 23 / 28 / 33 / 39 / 46 / alkoxycarbonyl<(1-6)> / CO2H / alkylaminocarbonyl<(1-6)> / dialkylaminocarbonyl<(1-6)> / (SC Me) / (EX OMe / OEt / Et / Ph / CH2CH=CH2 / hexyl / CH2Ph / CF3 / F / Pr-i)

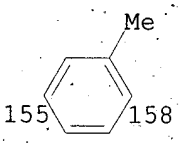




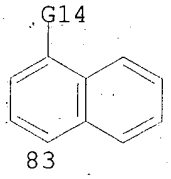
G2 = alkenylene<(2-6)> / alkynylene<(2-6)>
G3 = aryl<(6-10)> (SO) / heteroaryl<(2-9)> (SO)
G4 = NH / S / O
G5 = alkyl<(1-6)> (SO) / aryl<(6-10)> (SO) / heteroaryl<(2-9)> (SO) / acyl
G6 = alkyl<(1-6)> (SO)
G7 = H / alkyl<(1-6)> (SO)
G8 = **arylene<(6-10)> (SO (1-) G11)** / heteroarylene<(2-9)> (SO (1-) G11) / (SC phenylene) / (EX 143-10 146-74 / 149-10 151-74 / 155-10 158-74)

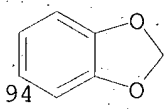


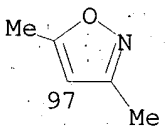


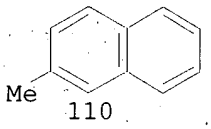


G9 = alkylene<(1-6)> / **(SC CH2)** / (EX CH2CH2)
G10 = **aryl<(6-10)> (SO (1-) G11)** / heteroaryl<(2-9)> (SO (1-) G11) / (SC pyridyl (SO (1-) G13) / thienyl (SO (1-) G13) / pyrazinyl (SO (1-) G13) / pyrimidinyl (SO (1-) G13) / pyridazinyl (SO (1-) G13) / thiazolyl (SO (1-) G13) / oxazolyl (SO (1-) G13) / Ph (SO (1-) G12)) / (EX 83 / 94 / 97 / 2-naphthyl / 110)

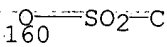




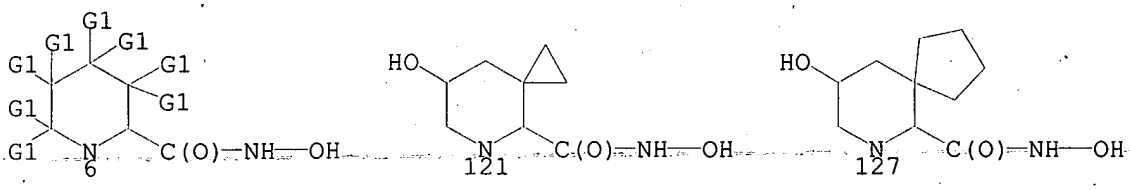




G11 = X / CN / alkyl<(1-6)> (SO (1-) F) / OH / alkyl<(1-6)> (SR OH) / alkoxy<(1-6)> (SO (1-) F) / alkyl<(1-6)> (SR alkoxy<(1-6)>) / **CO2H** / alkoxycarbonyl<(1-6)> / alkyl<(1-6)> (SR CO2H) / alkyl<(1-6)> (SR alkoxycarbonyl<(1-6)>) / alkylcarbonyloxy<(1-6)> / alkyl<(1-6)> (SR alkylcarbonyloxy<(1-6)>) / CHO / alkyl<(1-6)> (SR CHO) / alkylcarbonyl<(1-6)> / alkyl<(1-6)> (SR alkylcarbonyl<(1-6)>) / NO2 / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / alkyl<(1-6)> (SR NH2) / alkyl<(1-6)> (SR alkylamino<(1-6)>) / alkyl<(1-6)> (SR dialkylamino<(1-6)>) / CONH2 / alkylaminocarbonyl<(1-6)> / dialkylaminocarbonyl<(1-6)> / alkyl<(1-6)> (SR CONH2) / alkyl<(1-6)> (SR alkylaminocarbonyl<(1-6)>) / alkyl<(1-6)> (SR dialkylaminocarbonyl<(1-6)>) / NHCHO / alkylcarbonylamino<(1-6)> / alkyl<(1-6)> (SR NHCHO) / alkyl<(1-6)> (SR alkylcarbonylamino<(1-6)>) / alkylthio<(1-6)> / alkylsulfinyl<(1-6)> / alkylsulfonyl<(1-6)> / alkylsulfonylamino<(1-6)> / SO2NH2 / alkyl<(1-6)> (SR SO2NH2) / alkyl<(1-6)> (SR alkylaminosulfonyl<(1-6)>) / alkyl<(1-6)> (SR dialkylaminosulfonyl<(1-6)>) / 160 / alkylsulfonyloxy<(1-6)> / Ph / alkyl<(1-6)> (SR Ph) / cycloalkyl<(3-10)> / Hy<EC (2-9) C, AR (0), BD (ALL) SE> / heteroaryl<(2-9)>



G12 = Me / F / CF3 / Pr-i / Et / (EX OMe / CN / Cl / Br / I / CO2Me / Bu-t / Ph)
G13 = X / alkyl<(1-6)> / alkoxy<(1-6)> / perfluoroalkyl<(1-3)> / (EX Cl / Me)
G14 = H / Me
G15 = 6 / (EX 121 / 127)



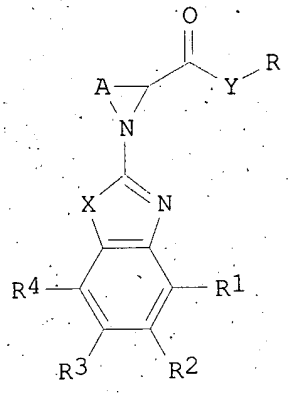
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted
NTE: addition ring derivatization also claimed

L3 ANSWER 20 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:137377 MARPAT
TITLE: Preparation of benzoxazolyl piperidines and analogs as rotamase enzyme inhibitors
INVENTOR(S): Kemp, Mark Ian; Palmer, Michael John; Sanner, Mark Allen; Wythes, Martin James
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005232	A1	20000203	WO 1999-IB1211	19990628
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338214	AA	20000203	CA 1999-2338214	19990628
AU 9942858	A1	20000214	AU 1999-42858	19990628
BR 9912330	A	20010417	BR 1999-12330	19990628
EP 1100797	A1	20010523	EP 1999-963123	19990628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002521382	T2	20020716	JP 2000-561188	19990628
NO 2001000322	A	20010315	NO 2001-322	20010119

PRIORITY APPLN. INFO.: GB 1998-15880 19980721
WO 1999-IB1211 19990628

GI



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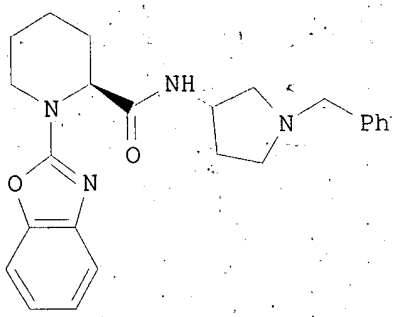
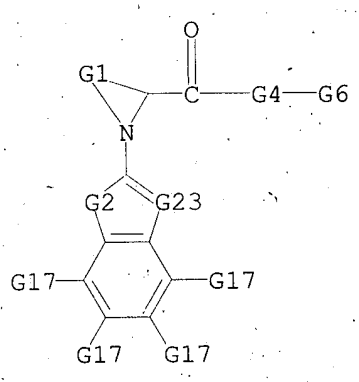


II

AB Title compds. (I) [wherein A = (un)substituted unbranched C3-C5 alkylene; X and Y = independently O, S, NH, or N-alkyl; R = (un)substituted, C-linked, 4- to 6-membered, non-arom., heterocyclic ring contg. 1 N; R1-R4 = independently H, halo, (cyclo)alkyl, haloalkyl, (cyclo)alkoxy, CONR5R6, cycloalkylalkylene, cycloalkylalkoxy, or CO2R7; R5 and R6 = independently H, alkyl, or taken together = unbranched alkylene; R7 = alkyl] were prepd. as rotamase enzyme inhibitors, particularly FKBP-12 and FKBP-52 inhibitors. Thus, (2S)-1-(1,3-benzoxazol-2-yl)-2-piperidinecarboxylic acid (prepn. given) was amidated with (3S)-1-benzylpyrrolidine-3-ylamine in the presence of 1-hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.HCl in CH2Cl2 to yield II. Twenty-one compds. of the invention demonstrated inhibitory activity against human recombinant FKBP-12 in a coupled colorimetric PPIase in vitro assay with IC50 values below 1200 nM, and II inhibited the rotamase enzyme FKBP-52 in a similar assay with IC50 = 2790 nM. As neurotrophic agents, the invention compds. promote neuronal regeneration and outgrowth and are useful for the treatment of neurodegenerative diseases or other disorders involving nerve damage.

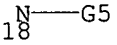
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1



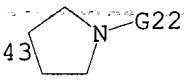
G1 = (3-5) CH2 (SO alkyl<(1-6)>)
G2 = O / S / 13

G3 = H / alkyl<(1-6)>
G4 = O / S / NH / 18



18

G5 = alkyl<(1-6)>
G6 = Hy<EC (4-6) A (1) Q (1) N (0) OTHERQ (3-5) C, AN (1-) C, RC (1), RS (1) M4 (1) X6> (SO (1-3) G7) / (SC 43 / 170 / 178)



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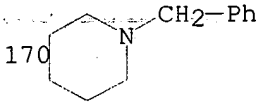

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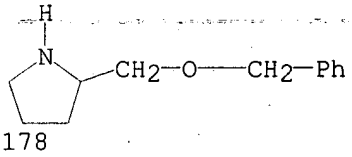
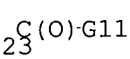


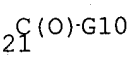
178

G7 = alkyl<(1-6)> (SO (1-2) G12) / alkenyl<(2-6)> (SO (1-2) G12) / cycloalkyl<(3-7)> / Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / alkoxycarbonyl<(1-6)> / 23



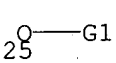
23

G8 = alkyl<(1-6)> (SO (1-) G25) / alkoxy<(1-6)> / F / Cl / Br / I / **21** / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino



21

G9 = alkyl<(1-6)> (SO (1-) G25) / alkoxy<(1-6)> / F / Cl / Br / I / Ph / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G10 = NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G11 = Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino / Ph (SO (1-3) G8)
G12 = cycloalkyl<(3-7)> / Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / **25** / 29



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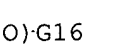
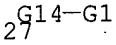


29

G13 = **Ph (SO (1-3) G8)** / 27



27

G14 = **CH2** / CHMe / CH2CH2
G15 = **Ph (SO (1-3) G8)**

G16 = Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino

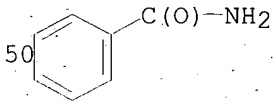
G17 = H / F / Cl / Br / I / alkyl<(1-6)> (SO (1-) G25) / cycloalkyl<(3-7)> / alkoxy<(1-6)> / 35 / cycloalkyloxy<(3-7)> / 37 / 41 / alkoxycarbonyl<(1-6)> / (SC Br)

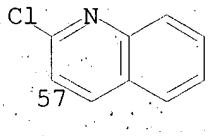
35 C(O)G10 37 G18—G19 41 O—G18—G19

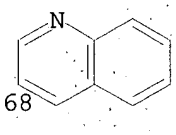
G18 = alkylene<(2-4)>

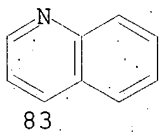
G19 = cycloalkyl<(3-7)>

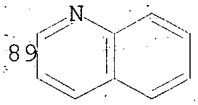
G20 = Ph / pyridyl / 50 / 57 / 68 / 83 / 89





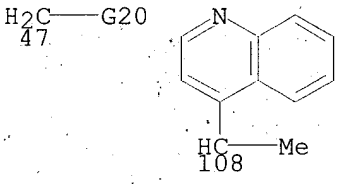


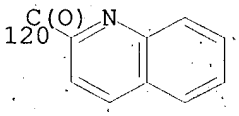


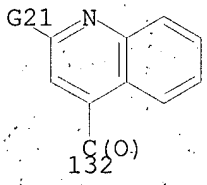


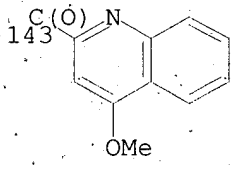
G21 = Ph / piperidino / Cl

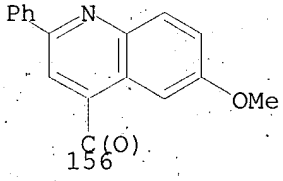
G22 = 47 / 108 / 120 / 132 / 143 / 156 / 168

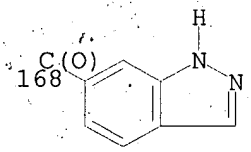












G23 = N / 188

N 188 G24

G24 = R<TX "pharmaceutically acceptable salt"> / (SC 190)

H—Cl
190

G25 = F / Cl / Br / I
DER: or pharmaceutically acceptable salts
MPL: claim 1

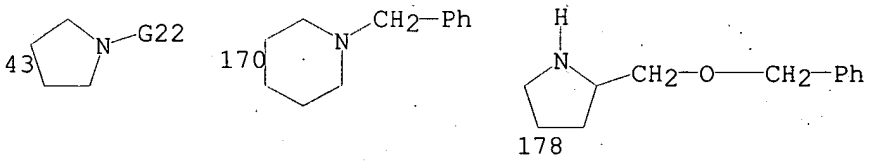
MSTR 4

G4—G6

G4 = OH / SH / NH2 / 18

HN—G5
18

G5 = alkyl<(1-6)>
G6 = Hy<EC (4-6) A (1) Q (1) N (0) OTHERQ (3-5) C, AN (1-) C, RC (1), RS (1) M4 (1) X6> (SO (1-3) G7) / (SC 43 / 170 / 178)



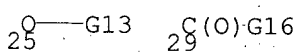
G7 = alkyl<(1-6)> (SO (1-2) G12) / alkenyl<(2-6)> (SO (1-2) G12) / cycloalkyl<(3-7)> / Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / alkoxycarbonyl<(1-6)> / 23

C(O)G11
23

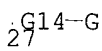
G8 = alkyl<(1-6)> (SO (1-) G25) / alkoxy<(1-6)> / F / Cl / Br / I / **21** / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino

C(O)G10
21

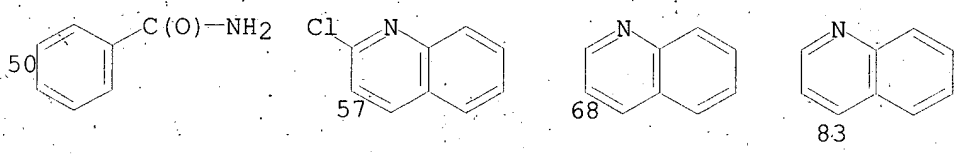
G9 = alkyl<(1-6)> (SO (1-) G25) / alkoxy<(1-6)> / F / Cl / Br / I / Ph / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G10 = NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G11 = Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino / Ph (SO (1-3) G8)
G12 = cycloalkyl<(3-7)> / Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / **25** / 29

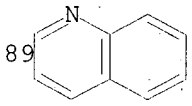


G13 = **Ph (SO (1-3) G8)** / 27

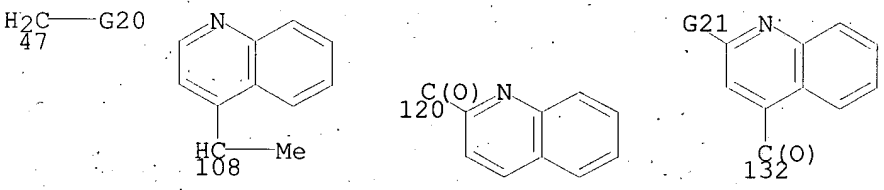


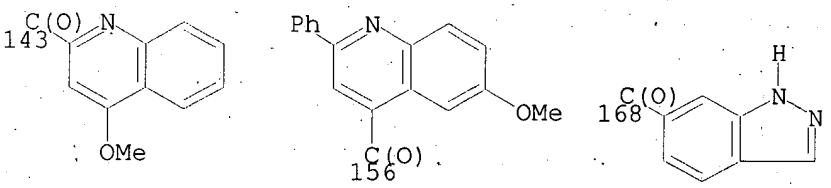
G14 = **CH2** / CHMe / CH2CH2
G15 = **Ph (SO (1-3) G8)**
G16 = Ph (SO (1-3) G8) / Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / NH2 / alkylamino<(1-6)> / dialkylamino<(1-6)> / azetidino / pyrrolidino / piperidino
G20 = Ph / pyridyl / 50 / 57 / 68 / 83 / 89





G21 = Ph / piperidino / Cl
G22 = 47 / 108 / 120 / 132 / 143 / 156 / 168





G25 = F / Cl / Br / I
MPL: claim 29

L3 ANSWER 21 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:117565 MARPAT
TITLE: Pentamidine and analogs as imidazoline receptor-binding compounds, and library screening method
INVENTOR(S): Tidwell, Richard R.; Hall, James E.; Wood, Dorothy H.

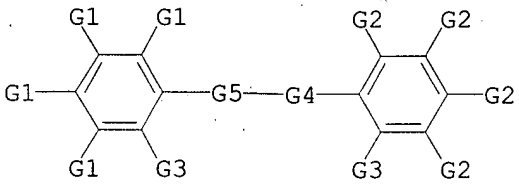
Searched by Barb O'Bryen, STIC 308-4291

PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

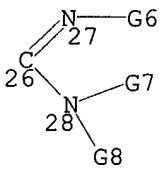
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004893	A2	20000203	WO 1999-US14428	19990625
WO 2000004893	A3	20000629		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338279	AA	20000203	CA 1999-2338279	19990625
AU 9948327	A1	20000214	AU 1999-48327	19990625
EP 1097382	A2	20010509	EP 1999-931916	19990625
R: CH, DE, FR, GB, IT, LI				
JP 2002527357	T2	20020827	JP 2000-560886	19990625
PRIORITY APPLN. INFO.:			US 1998-120584	19980722
			WO 1999-US14428	19990625

AB Pentamidine and analogs thereof have activity as imidazoline receptor binding compds. A method of binding the imidazoline receptor comprises contacting a bis-benzene to the imidazoline receptor in an amt. effective to bind to the receptor, wherein the bis-benzene contains at least one amidine group (e.g., one or two). The contacting step may be carried out in vivo or in vitro. Contacting may be carried out with individual active compds. or with libraries of active compds.

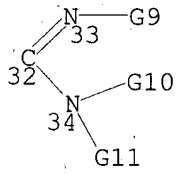
MSTR 6



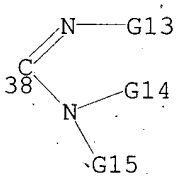
G1 = (3-) H / alkyl<(1-6)> (SO NH2) / alkoxy<(1-6)> / NO2 / NH2 / F / Cl / Br / I / OH / **CO2H** / 26



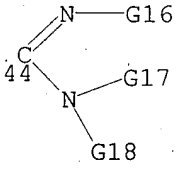
G2 = (3-) H / alkyl<(1-6)> (SO NH2) / alkoxy<(1-6)> / NO2 / NH2 / F / Cl / Br / I / OH / **CO2H** / 32



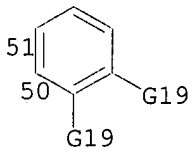
G3 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl / F / Cl / Br / I
G4 = **O** / S / NH
G5 = **(1-8) CH2**
G6 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G7 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G8 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G9 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G10 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G11 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G12 = NH2 / alkylamino / OH / alkoxy
G13 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G14 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G15 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G16 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G17 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G18 = H / alkyl<(1-6)> (SO G12) / alkoxy<(1-6)> / cycloalkyl<(3-8)> / aryl
G19 = (1) 38 / H



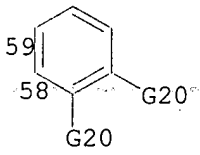
G20 = (1) 44 / H



G6 +G7 = alkylene<EC (2-4) C, DC (0) M3> / 50-27 51-28



G9 +G10= alkylene<EC (2-4) C, DC (0) M3> / 58-33 59-34



G13+G14= alkylene<EC (2-4) C, DC (0) M3> / o-C6H4
G16+G17= alkylene<EC (2-4) C, DC (0) M3> / o-C6H4
DER: or pharmaceutically acceptable salts
MPL: claim 13
NTE: the compound has at least one amidine group

L3 ANSWER 22 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:102202 MARPAT
TITLE: Preparation of pyridinioalkylindoles and related compounds as bacterial NAD synthetase inhibitors.
INVENTOR(S): Brouillette, Wayne J.; Muccio, Donald; Jedrzejas, Mark J.; Brouillette, Christie G.; Devedjiev, Yancho; Cristofoli, Walter; Delucas, Lawrence J.; Garcia, Jose Gabriel; Schmitt, Laurent
PATENT ASSIGNEE(S): The UAB Research Foundation, USA
SOURCE: PCT Int. Appl., 200 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936422	A1	19990722	WO 1999-US810	19990114
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CA 2317439	AA	19990722	CA 1999-2317439	19990114
EP 1047692	A1	20001102	EP 1999-900821	19990114
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JP 2002509149	T2	20020326	JP 2000-540138	19990114
CA 2341506	AA	20000302	CA 1999-2341506	19990630
WO 2000010996	A1	20000302	WO 1999-US14839	19990630
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MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9949639	A1	20000314	AU 1999-49639	19990630
EP 1109805	A1	20010627	EP 1999-933622	19990630
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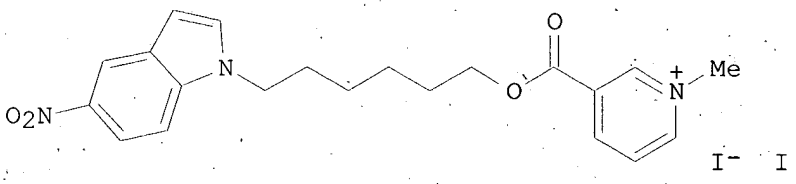
JP 2002523412	T2	20020730	JP 2000-566269	19990630
AU 9920317	A1	19990802	AU 1999-20317	19990802
US 6500852	B1	20021231	US 2000-617258	20000714
PRIORITY APPLN. INFO.:			US 1998-71399P	19980114
			US 1998-97880P	19980825
			WO 1999-US810	19990114
			WO 1999-US14839	19990630

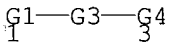
GI



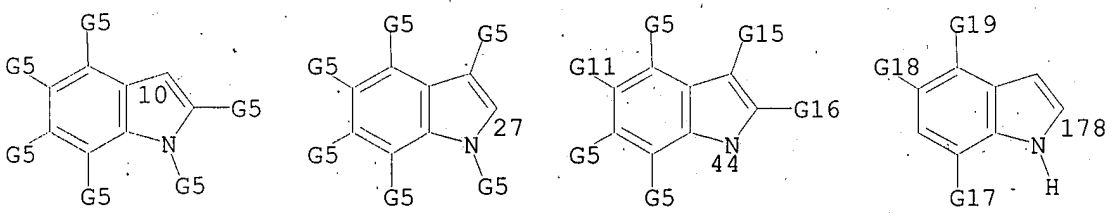
AB Title compds. e.g. R1R2R3Ar(R4R5L)nArR6R7 [Ar = aryl; n = 1-12; R1-R7 = H, (substituted) cyclic or aliph., branched or unbranched group; L = cyclic or aliph., branched or unbranched alkyl, alkenyl, alkynyl which may contain heteroatoms], were prepd. Thus, 5-nitroindole in DME was added to NaH in DME followed by heating to reflux, cooling, treatment with 6-bromohexyl acetate, and 18 h reflux to give 91.2% 6-[N-(5-nitroindolyl)]hexyl acetate. The product was sapond. with K2CO3 in MeOH/H2O (91.6%) followed by stirring with nicotinic acid, DCC, and DMAP in CH2Cl2 followed by heating with MeI to give title compd. (I). I at 0.2 mM gave 46.43% inhibition of bacterial NAD synthetase.

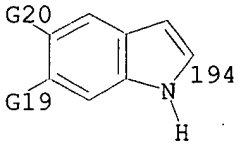
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

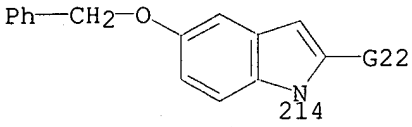
MSTR 1

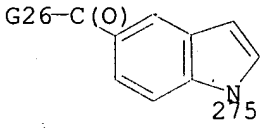


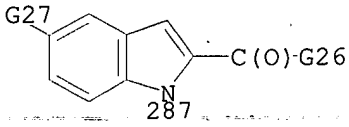
G1 = aryl (SO (1-3) G2) / **heteroaryl<EC (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-3) G2)** / (SC 10 / 27 / 44 / 178 / 194 / 214 / 275 / 287 / 298 / 309 / 321 / 333 / 345 / 356 / 368 / 375 / 395)

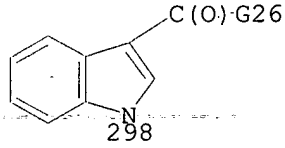


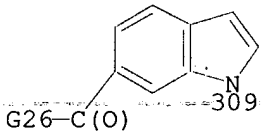


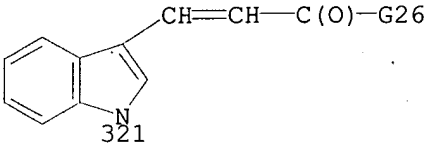


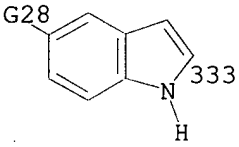


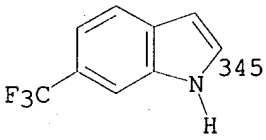


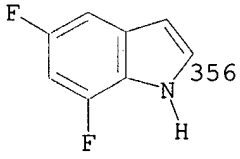


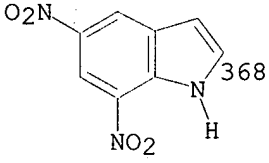


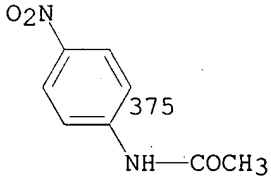


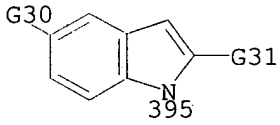






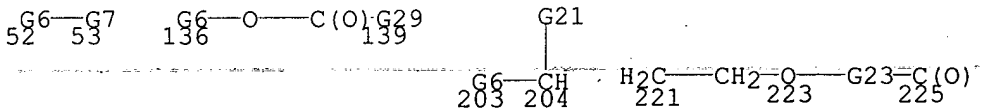


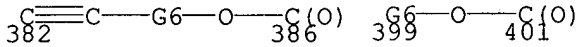




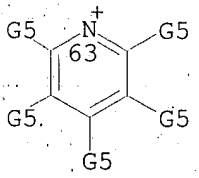
G2 = Cb (SO) / Ak (SO) / R / (SC alkyl<(1-24)> / alkenyl<(2-24)> / alkynyl<(2-24)> / aryl / OH / acyl / NO2 / NH2 / C(NH)NH2 / NHC(NH)NH2 / **CO2H** / CONH2 / SO3H / X)

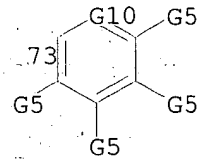
G3 = R<TX "linker optionally containing heteroatoms"> / alkylene<(1-24)> (SO (1-2) G2) / alkenylene<(2-24)> (SO (1-2) G2) / alkynylene<(2-24)> (SO (1-2) G2) / (SC G6 / 52-1 53-3 / 136-1 139-3 / 399-1 401-3 / 203-1 204-3 / 221-1 225-3 / 382-1 386-3)

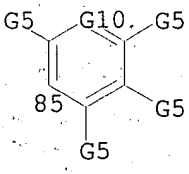


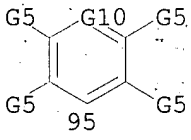


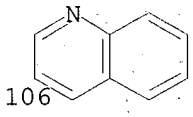
G4 = aryl (SO (1-2) G2) / **heteroaryl<EC (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-2) G2)** / (SC Ph (SO (1-2) G9) / 63 / pyridyl (SO (1-2) G9) / 73 / 85 / 95 / 106 / 116 / 127 / 131 / 142 / 153 / 162 / 201 / 235 / 239 / 249 / 258 / biphenylyl (SO (1) NMe2))

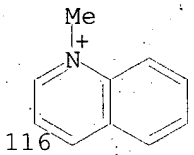


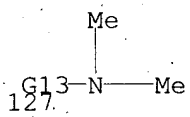


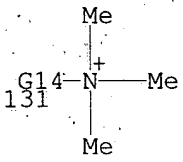


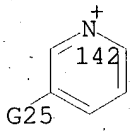


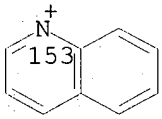


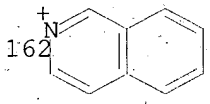


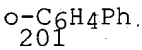


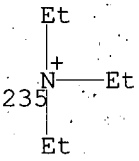


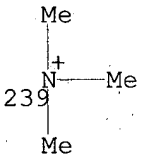


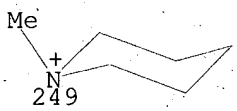


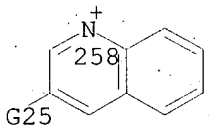




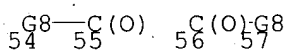




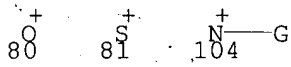




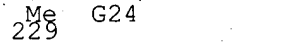
G5 = H / Cb (SO) / Ak (SO) / R
G6 = **(1-12) CH2**
G7 = NH (SO) / **O** / S / 54-52 55-3 / 56-52 57-3 / C(O)



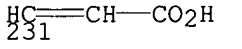
G8 = O / NH (SO)
G9 = Cb (SO) / Ak (SO) / R
G10 = 80 / 81 / 104



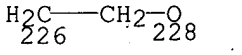
G11 = H / Cb (SO) / Ak (SO) / R / (SC OMe / OCH2Ph / NO2 / CO2H)
G12 = Cb (SO) / Ak (SO) / R / (SC Me / 229)



G13 = m-C6H4 / p-C6H4
G14 = m-C6H4 / p-C6H4
G15 = H / Cb (SO) / Ak (SO) / R / (SC CO2H / 231)



G16 = H / Cb (SO) / Ak (SO) / R / (SC CO2H)
G17 = H / F / NO2
G18 = H / Me / CF3 / NO2 / Ph / Bu-n / Pr-i / F / OPh / CPh3 / CO2Me / OMe / CO2H / COMe / COPh
G19 = H / CF3
G20 = H / OPh / Pr-i / COMe / COPh
G21 = Ph / H
G22 = H / CO2Me
G23 = (0-3) 226-223 228-225



G24 = R<TX "anion", CH (1) ->
G25 = carboxylate / CO2Me
G26 = OCH2Ph / OMe / OH
G27 = H / OCH2Ph / OMe
G28 = H / Me / Bu-n / Pr-i / Ph / NO2 / CPh3 / F / OPh / COPh / CF3 / COMe / OMe / CO2Me / CO2H
G29 = (1-2) CH2
G30 = H / OCH2Ph
G31 = H / CO2Me
MPL: claim 2

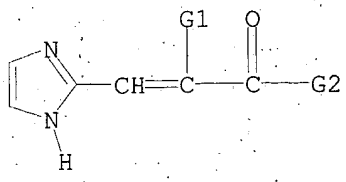
L3 ANSWER 23 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:73654 MARPAT
TITLE: Imidazole derivatives and medicines comprising the same as active ingredient
INVENTOR(S): Shioiri, Noriaki; Mikami, Tadashi; Morimoto, Shinichi; Yamazaki, Kazuo; Naito, Hiroyuki; Okawa, Junji; Kawamoto, Noriyuki; Hasegawa, Hiroshi; Tachibana, Koichi; Sato, Susumu; Yokoyama, Toshio
PATENT ASSIGNEE(S): Ssp Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 924202	A1	19990623	EP 1998-122468	19981126
EP 924202	B1	20020529		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 11236377	A2	19990831	JP 1998-317173	19981109
US 6071943	A	20000606	US 1998-200750	19981130
CN 1222514	A	19990714	CN 1998-125564	19981216

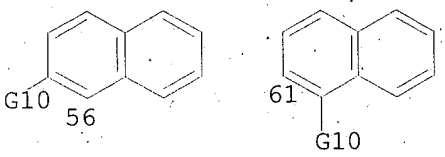
PRIORITY APPLN. INFO.: JP 1997-346215 19971216
AB Disclosed herein are imidazole derivs., RCH:CR1COC6H2R2R3R4 (R = 2-imidazolyl, R1 = H, alkyl, alkoxy, alkoxycarbonyl; R2, R3, R4 are the same or different from one another and are independently H, halogen, alkyl, haloalkyl, hydroxy, alkoxy). The compds. specifically suppress the prodn. of a particular cytokine and is hence useful as an active ingredient for immune function modulators and the like.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

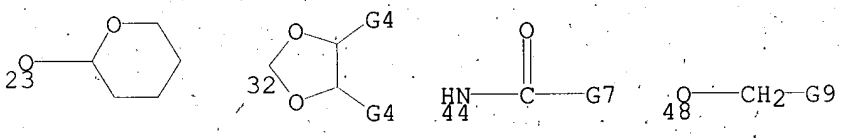
MSTR 1



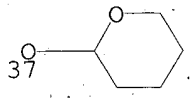
G1 = H / alkyl / cycloalkyl / alkoxy / alkoxycarbonyl
G2 = Ph (SR (-3) G3) / **aryl<EC (7-) C, AR (1-), BD (6-) N, RC (2), RS (1-) E6> (SO (1-) G3)** / (EX 56 / 61)



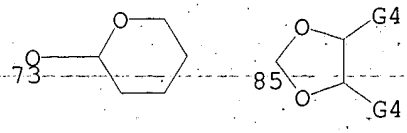
G3 = F / Cl / Br / I / alkyl (SO (1-) G5) / cycloalkyl / OH / alkoxy / **CO2H** / NO2 / 23 / alkoxy (SR alkoxy) / alkoxycarbonyl / CN / tetrazolyl / Ph (SO (1-) G6) / OPh (SO (1-) G6) / **48** / NH2 (SO) / 32 / (EX alkylamino<(1-6)> / dialkylamino<(1-6)> / 44 / alkylsulfonylamino<(1-6)> / arylsulfonylamino / NHCOPh (SO G8))



G4 = H / R
G5 = F / Cl / Br / I
G6 = R / (EX alkyl<(1-6)> (SO (1-) G5) / alkoxy<(1-6)> / F / Cl / Br / I / alkoxy<(1-6)> (SR alkoxy<(1-6)>) / 37 / **CO2H** / alkoxycarbonyl<(1-6)> / CN / OH / NO2 / tetrazolyl / NH2 (SO))



G7 = H / Ak<(1-6)> / R
G8 = R / alkoxy (SR Ph)
G9 = **Ph (SO (1-) G6)**
G10 = H / F / Cl / Br / I / alkyl (SO (1-) G5) / cycloalkyl / OH / alkoxy / CO2H / NO2 / 73 / alkoxy (SR alkoxy) / alkoxycarbonyl / CN / tetrazolyl / Ph (SO) / OPh (SO) / OCH2Ph (SO) / NH2 (SO) / 85

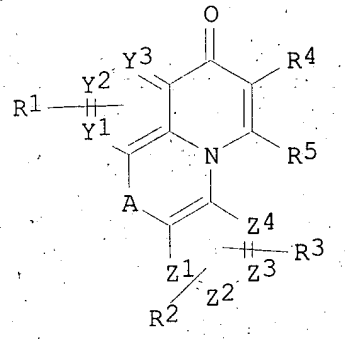


DER: or salts
MPL: claim 1

L3 ANSWER 24 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:18932 MARPAT
TITLE: Preparation and formulation of heterocyclic compounds as cyclic GMP phosphodiesterase inhibitors
INVENTOR(S): Ohashi, Masayuki; Nishida, Hidemitsu; Shudo, Toshiyuki
PATENT ASSIGNEE(S): Mochida Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 253 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928319	A1	19990610	WO 1998-JP5350	19981127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9810766	A	19990525	ZA 1998-10766	19981125
CA 2311947	AA	19990610	CA 1998-2311947	19981127
AU 9912617	A1	19990616	AU 1999-12617	19981127
AU 746883	B2	20020502		
BR 9815070	A	20001003	BR 1998-15070	19981127
EP 1048666	A1	20001102	EP 1998-955965	19981127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2000002696	A	20000724	NO 2000-2696	20000526
US 6476021	B1	20021105	US 2000-580657	20000526
PRIORITY APPLN. INFO.:			JP 1997-344164	19971128
			WO 1998-JP5350	19981127

GI



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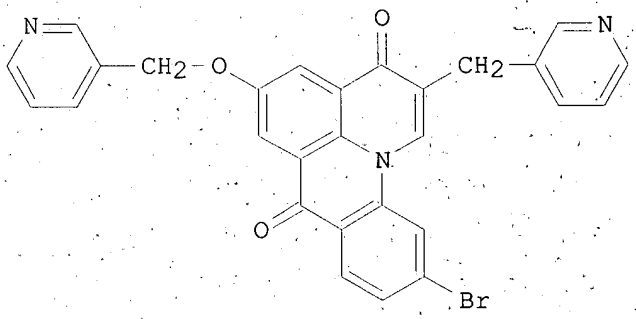
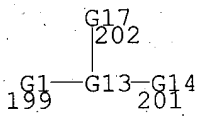


II

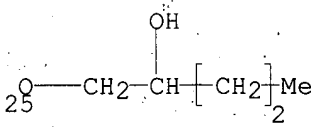
AB The title compds. I [A = single bond, methylene, etc.; R1 = H, halo, etc.; R2 = H, halo, (protected) amino; etc.; R3 = H, halo, (protected) OH, etc.; R4 = H, halo, etc.; R5 = H, methyl; Y1 - Y3, Z1 - Z4 = methine, N] are prepd. I are useful as preventives and/or remedies for pulmonary hypertension, ischemic heart diseases, erectile insufficiency, female sexual dysfunction or diseases against which cGMP-PDE inhibitory effects are efficacious. The title compd. II in vitro showed IC50 of 0.0018 .mu.M against cyclic GMP phosphodiesterase.

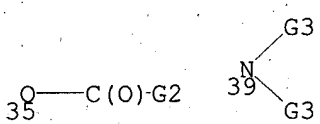
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

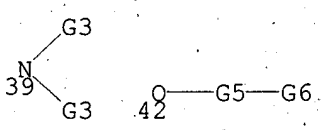
MSTR 1

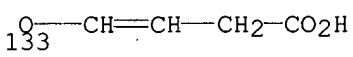


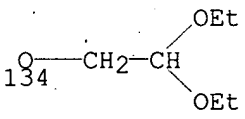
G1 = H / F / Cl / Br / CN / CO2H (SO) / CH2CO2H (SO) / alkoxycarbonyl<(1-4)> / CONH2 / NHCOMe / 133 / 25 / 134 / OH (SO) / SH (SO) / OCHO / alkylcarbonyloxy<(1-3)> / 35 / alkyl<(1-4)> (SO (-1) OH) / 39 / alkylthio<(1-3)> (SO (-1) G4) / 143 / **42**

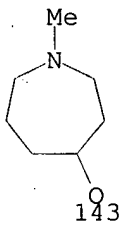




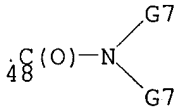


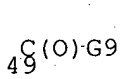


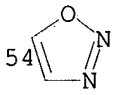


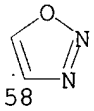


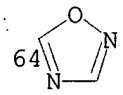
G2 = Ph / pyridyl
G3 = H / alkyl<(1-4)>
G4 = OH / CO2H / Ph / pyridyl
G5 = **(1-6) CH2**
G6 = H / CO2H / alkoxy<(1-2)> (SO (-1) OH) / alkoxycarbonyl<(1-6)> / 48 / CHO / alkylcarbonyl<(1-3)> (SO G8) / 49 / OH / SH / 145 / Hy<EC (1-) N, AN (1) N> (SO) / **Ph (SO (1-2) G23)** / pyridyl (SO (-1) G11) / pyrazinyl / pyrimidinyl / furyl / thienyl / 54 / 58 / 64 / 72 / 73 / 79 / 90 / 154 / 164 / morpholino

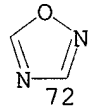


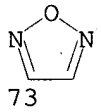


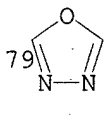


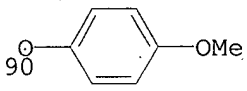


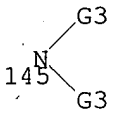


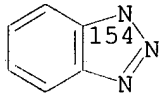


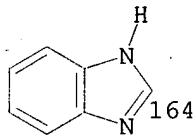




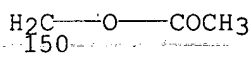




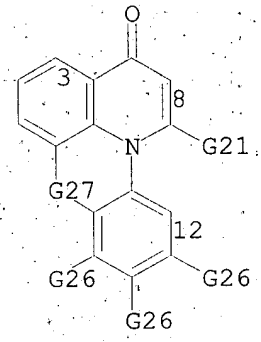


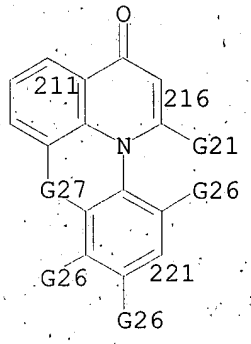


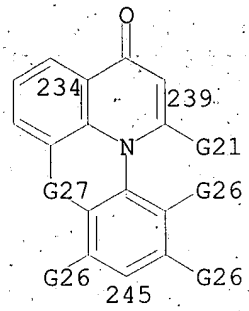
G7 = H / CH2OH / alkyl<(1-2)>
G8 = OH / SH
G9 = piperidino (SO (-1) G10) / morpholino
G10 = CO2H / alkoxycarbonyl<(1-2)>
G11 = F / Cl / Br / OH / SH / alkoxy<(1-2)> / alkylthio<(1-2)> / alkoxycarbonyl<(1-4)> / NHCOMe / CO2H / NH2 / CN / NO2 / loweralkylamino / diloweralkylamino / CONH2 / alkyl<(1-4)> / CH2OH / 150

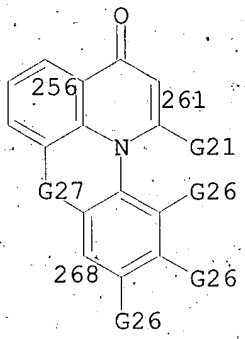


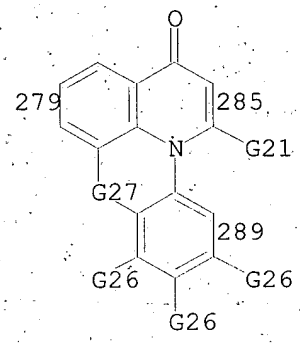
G13 = 3-199 8-202 12-201 / 211-199 216-202 221-201 / 234-199 239-202 245-201 / 256-199 261-202 268-201 / 279-199 285-202 289-201 / 301-199 307-202 312-201 / 323-199 329-202 335-201 / 345-199 351-202 358-201 / 366-199 373-202 377-201 / 388-199 395-202 400-201 / 410-199 417-202 423-201 / 432-199 439-202 446-201 / 454-199 461-202 467-201 / 476-199 483-202 489-201 / 498

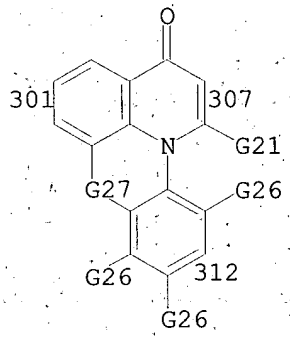

O
3
8
N
G21
G27
12
G26
G26
G26

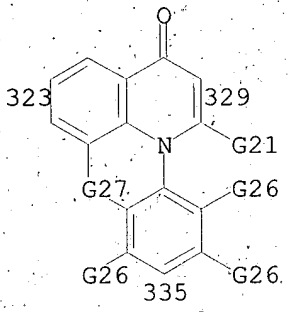

O
211
216
N
G21
G27
G26
G26
221
G26

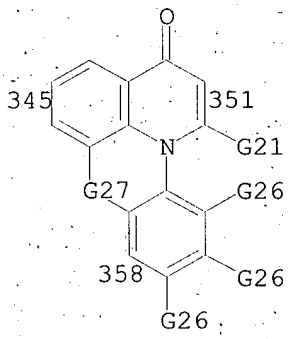

O
234
239
N
G21
G27
G26
G26
245
G26

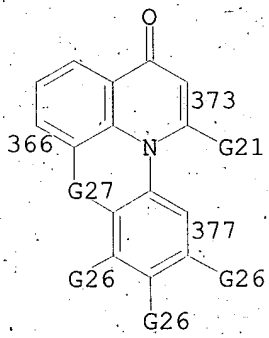

O
256
261
N
G21
G27
G26
268
G26
G26

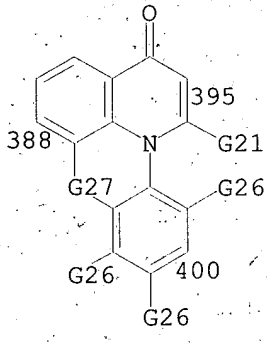

O
279
285
N
G21
G27
289
G26
G26
G26

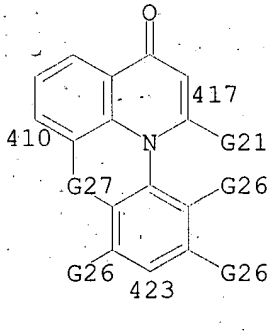

O
301
307
N
G21
G27
G26
G26
312
G26

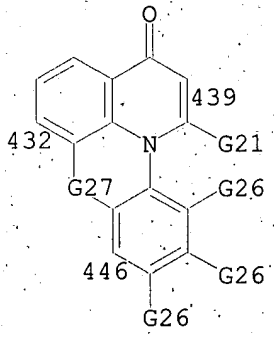

O
323
329
N
G21
G27
G26
G26
335
G26

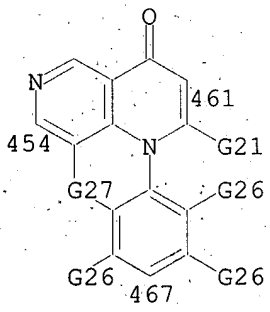

O
345
351
N
G21
G27
G26
358
G26
G26

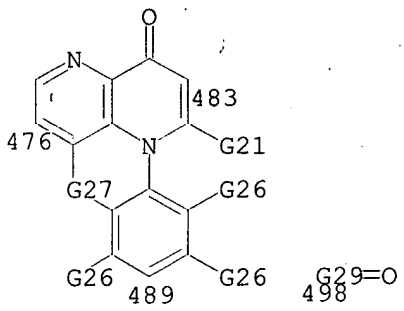

O
366
373
N
G21
G27
377
G26
G26
G26


O
388
395
N
G21
G27
G26
G26
400
G26

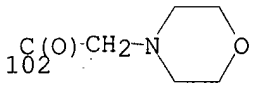

O
410
417
N
G21
G27
G26
G26
423
G26


O
432
439
N
G21
G27
G26
446
G26
G26

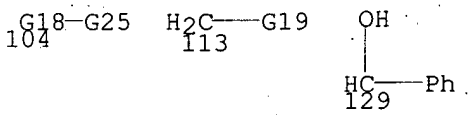

O
N
454
461
N
G21
G27
G26
G26
467
G26



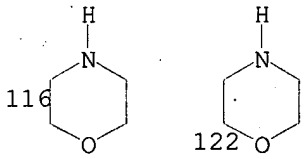
G14 = H / F / Cl / Br / OH (SO) / SH (SO) / NH2 (SO) / CN / NO2 / CF3 / OCF3 / **CO2H (SO)** / 102 / OCHO / alkylcarbonyloxy<(1-3)> / alkyl<(1-4)> / alkylthio<(1-3)> (SO (-1) G15) / alkoxy<(1-4)> (SO (-1) G24)



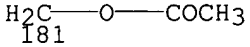
G15 = OH / CO2H / Ph / pyridyl
G17 = H / F / Cl / Br / 104 / alkyl<(1-2)> (SO cycloalkyl<(3-6)>) / 113 / COPh / 129



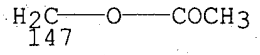
G18 = O / NH / NMe
G19 = Ph (SO (1-2) G20) / pyridyl (SO (-1) G20) / morpholino / 116 / 122 / triazolyl / furyl / thienyl / pyrimidinyl / pyrazinyl / pyrrolyl / imidazolyl / quinolinyl / indolyl / naphthyl



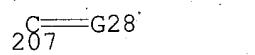
G20 = F / Cl / Br / OH / SH / alkoxy<(1-2)> / alkylthio<(1-2)> / alkoxycarbonyl<(1-4)> / NHCOMe / CO2H / NH2 / CN / NO2 / loweralkylamino / diloweralkylamino / CONH2 / alkyl<(1-4)> / CH2OH / 181



G21 = H / Me
G23 = F / Cl / Br / OH / SH / alkoxy<(1-2)> / alkylthio<(1-2)> / alkoxycarbonyl<(1-4)> / NHCOMe / **CO2H** / NH2 / CN / NO2 / NH2 / loweralkylamino / diloweralkylamino / CONH2 / alkyl<(1-4)> / CH2OH / 147



G24 = alkoxycarbonyl<(1-4)> / OH / CO2H / Ph / pyridyl
G25 = Ph (SO (1-2) G20)
G26 = H / F / Cl / Br / OH (SO) / alkoxy<(1-4)>
G27 = NULL / CH2 (SO) / 207 / O / S / S(O) / SO2 / NH (SO)



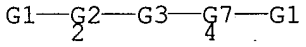
G28 = O / NH (SO)
G29 = **Hy<EC (1-) N (0-) O (0-) S (0) OTHERQ, AR (1-), BD (6-) N, RC (4), RS (0-1) E5 (3-4) E6 (0) OTHER> (SO)**
DER: or salts
MPL: claim 1
NTE: substitution is restricted

L3 ANSWER 25 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:88106 MARPAT
TITLE: Silver halide color photographic material
INVENTOR(S): Ishii, Fumio; Daiba, Shinichi; Oshiyama, Tomohiro; Hirabayashi, Shigeto; Iwai, Yoshiko
PATENT ASSIGNEE(S): Konica Corporation, Japan
SOURCE: Eur. Pat. Appl., 142 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

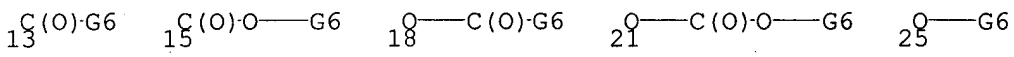
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 886179	A1	19981223	EP 1998-111048	19980616
EP 886179	B1	20011024		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 11007111	A2	19990112	JP 1997-158733	19970616
JP 11024219	A2	19990129	JP 1997-182358	19970708
JP 11044937	A2	19990216	JP 1997-214002	19970724
JP 11065048	A2	19990305	JP 1997-217563	19970812
JP 11065047	A2	19990305	JP 1997-222442	19970819
US 6010809	A	20000104	US 1998-166943	19980610
PRIORITY APPLN. INFO.:			JP 1997-158733	19970616
			JP 1997-182358	19970708
			JP 1997-214002	19970724
			JP 1997-217563	19970812
			JP 1997-222442	19970819

AB A silver halide color photog. material comprises a thermotropic liq. crystal compd. represented by the formula Y1A1(X1)mA2Y2 or Y1A1(X1)mA2(X2)nA3Y2 (A1-3 = an alicyclic or arom. group; X1, X2 = a bonding group; m, n = 0 or 1; Y1, Y2 = a substituent group). The color photog. material is improved in lightfastness of dye images and dye-forming efficiency.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

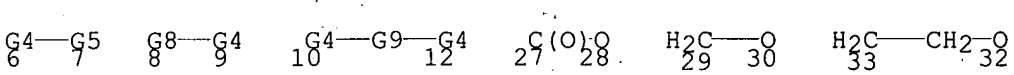
MSTR 1

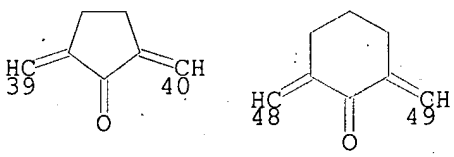


G1 = R<TX "substituent"> / (EX F / Cl / Br / CN / NO2 / OH / **CO2H** / 13 / 15 / 18 / 21 / 25 / Ak<(1-25)> / alkyl<(1-25)> / alkenyl<(2-25)> / alkynyl<(2-25)>)



G2 = Cb<AR (0)> (SO) / arylene (SO) / heteroarylene (SO) / **(EX phenylene)**
G3 = R<TX "bonding group"> / NULL / Cb<AR (0)> (SO) / arylene (SO) / heteroarylene (SO) / 6-2 7-4 / 8-2 9-4 / 10-2 12-4 / (EX phenylene / 27-2 28-4 / CH2CH2 / CH=CH / C(O) / CH2 / **29-2 30-4** / 33-2 32-4 / OCH2O / OCH2CH2O / 39-2 40-4 / 48-2 49-4)





G4 = R<TX "bonding group">
G5 = Cb<AR (0)> (SO) / arylene (SO) / heteroarylene (SO) / (EX phenylene)
G6 = Ak<(1-25)> / alkyl<(1-25)> / alkenyl<(2-25)> / alkynyl<(2-25)> / R
G7 = Cb<AR (0)> (SO) / arylene (SO) / heteroarylene (SO) / **(EX phenylene)**
G8 = Cb<AR (0)> (SO) / arylene (SO) / heteroarylene (SO) / (EX phenylene)
G9 = Cb<AR (0)> (SO) / arylene (SO) / heteroarylene (SO) / (EX phenylene)
MPL: claim 5

L3 ANSWER 26 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:81526 MARPAT
TITLE: Preparation of 4-[(4-piperazinobeznoyl)amino]phenyl(oxy)alkanoates as fibrinogen receptor antagonists
INVENTOR(S): Duggan, Mark E.; Egbertson, Melissa S.; Hartman, George D.; Young, Steven D.; Ihle, Nathan C.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 78 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

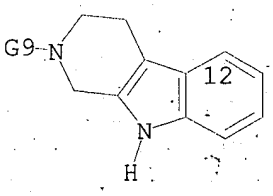
US 5854245 A 19981229 US 1997-883108 19970626
PRIORITY APPLN. INFO.: US 1997-883108 19970626
AB XYZAB [I; A = (un)substituted (hetero)arylene; B = O(CH2)mCO2R9, (CH2)nCO2R9, CHR8(CH2)pCO2R9, OCHR8(CH2)pCO2R9; R8 = H, OH, alkyl, alkoxy, aryl, etc.; R9 = H, (ar)alkyl, aryl, acylalkyl, etc.; X = (un)substituted heterocyclyl or -heteroaryl; Y = (un)substituted heterocyclylene or -(hetero)arylene; Z = bond, NH, CONH, CO, CH2CH2, etc.; m = 1-3; n,p = 0-3] were prepd. Thus, 4-(H2N)C6H4CO2Me was cyclocondensed with HN(CH2CH2Cl)2 and the N-protected and sapond. product amidated by 4-BrC6H4NH2 to give the bromobenzanilide which was condensed with CH2:CHCO2Me and the product converted in 3 addnl. steps to 4-RC6H4CONHC6H4(CH2CH2CO2H)-4 (R = piperazino). Data for biol. activity of I were given.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

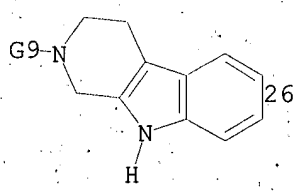
MSTR 2A

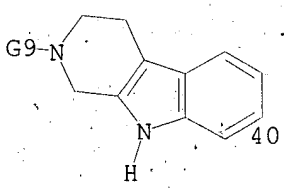
G7—G10—G13—G14
2 177

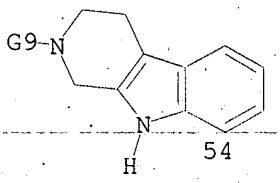
G1 = Hy<EC (-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G2)
G2 = F / Cl / Br / I / alkyl<(1-10)> / cycloalkyl<(3-8)> / Ph (SO (1-) G3) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X6> (SO (1-) G3) / alkyl<(1-8)> (SR (1-) G4) / NH2 / alkyl<(1-8)> (SR NH2) / alkylcarbonylamino<(1-3)> / NHCHO / alkyl<(1-8)> (SR G5) / alkyl<(1-8)> (SR alkylamino<(1-6)>) / alkylamino<(1-6)> / alkyl<(1-8)> (SR dialkylamino<(1-6)>) / alkoxy<(1-6)> / alkyl<(1-6)> (SR alkoxy<(1-6)>) / alkoxy<(1-6)> (SR (1-) G4) / alkyl<(1-6)> (SR G6) / **CO2H** / alkyl<(1-6)> (SR CO2H) / alkoxycarbonyl<(1-3)> / alkyl<(1-6)> (SR alkoxycarbonyl<(1-3)>) / alkoxy<(1-6)> (SR CO2H) / OH / alkyl<(1-6)> (SR OH)
G3 = NH2 / F / Cl / Br / I
G4 = Ph (SO (1-) G3) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X6> (SO (1-) G3)
G5 = NHCHO / alkylcarbonylamino<(1-3)>
G6 = alkoxy<(1-6)> (SR (1-) G4)
G7 = 3 / 12 / 26 / 40 / 54 / 72 / 85 / 98 / 111 / 128 / 141 / 154 / 167 / 232 / 245 / 258 / 271

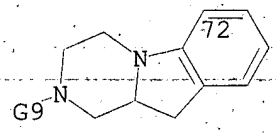
G1—G8
3

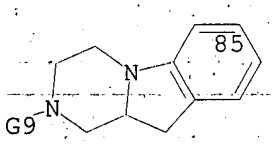


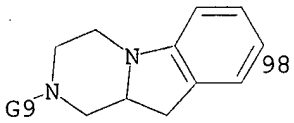


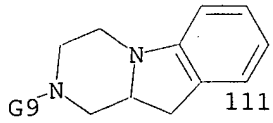


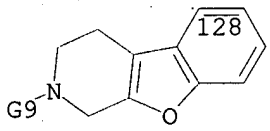


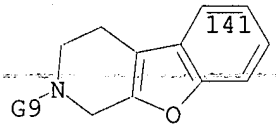


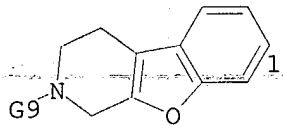


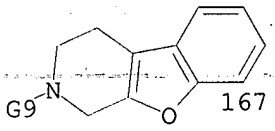


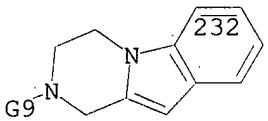


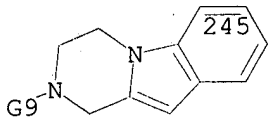


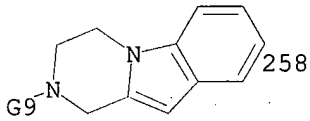


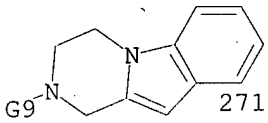




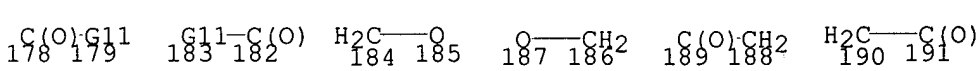


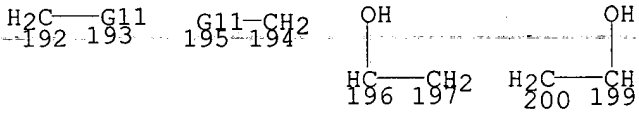




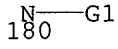


G8 = **Cb<EC (5-6) C, RC (1), RS (1) M5 (1) X6>**
(SO (1-) G2) / Hy<EC (5-6) A (1-3) Q (0-) N (0-) O (0-) S (0)
OTHERQ, RC (1), RS (1) M5 (1) X6> (SO (1-) G2)
G9 = H / R
G10 = 178-2 179-177 / 183-2 182-177 / CH2CH2 / CH=CH /
184-2 185-177 / 187-2 186-177 / 189-2 188-177 /
190-2 191-177 / 192-2 193-177 / 195-2 194-177 /
196-2 197-177 / 200-2 199-177





G11 = NH / 180



G12 = alkyl<(1-4)> / cycloalkyl<(3-6)>
G13 = **Cb<(5-10)> (SO (1-) G2)** /
Hy<EC (5-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ>
(SO (1-) G2)
G14 = 203 / 213 / 217

O—G15—C(O)—G16 G15—C(O)—G16 C(O)—G16
203 213 217

G15 = alkylene<(1-)> (SO)
G16 = OH / 207

O—G17
207

G17 = alkyl<(1-8)> / Ph (SO (1-) G3) /
heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RC (1), RS (1) M5 (1) X6> (SO (1-) G3) /
alkyl<(1-6)> (SR (1-) G4) / alkyl<(1-6)>
(SR alkylcarbonyloxy<(1-8)>) / alkyl<(1-6)> (SR 209) /
alkyl<(1-6)> (SR G18) / alkyl<(1-6)>
(SR alkylaminocarbonyl<(1-8)>) /
alkyl<(1-6)> (SR dialkylaminocarbonyl<(1-8)>)

O—C(O)—G4
209

G18 = alkylcarbonyloxy<(1-6)> (SR (1-) G4)
DER: or pharmaceutically acceptable salts
MPL: disclosure

L3 ANSWER 27 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:38195 MARPAT
TITLE: New nitromethyl ketones for use as aldose reductase inhibitors
INVENTOR(S): Lardy, Claude; Barbanton, Jacques; Dumas, Herve; Collonges, Francois; Durbin, Philipp
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9852906	A1	19981126	WO 1998-EP2353	19980421
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5932765	A	19990803	US 1997-955624	19971022
AU 9875280	A1	19981211	AU 1998-75280	19980421
AU 729996	B2	20010222		
EP 983226	A1	20000308	EP 1998-922757	19980421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
BR 9809677	A	20000711	BR 1998-9677	19980421
JP 2001526668	T2	20011218	JP 1998-549855	19980421

ZA 9804329	A	19990303	ZA 1998-4329	19980521
US 6043281	A	20000328	US 1999-257046	19990225
NO 9905724	A	19991122	NO 1999-5724	19991122
PRIORITY APPLN. INFO.:			EP 1997-108369	19970523
			US 1997-955624	19971022
			WO 1998-EP2353	19980421

AB R3Z(CR1R2)pEnA(X)COCH2NO2 [A = C6-C10 aryl or an optionally arom. three- to ten-membered heterocycle; X = halogen, cyano, alkyl, trifluoromethyl, alkoxy, trifluoromethoxy; p = 0-5; Z = bond, CONH, SO2NH, alkenylene, S, SO, SO2; n = 0, 1; R1, R2 = H, alkyl, cycloalkyl, CF3, alkoxy; CR1R2 = cycloalkylene; R3 = H, trialkylsilyl, (un)substituted alkyl, aryl, aryloxy, cycloalkyl, heterocyclic; E = (un)substituted CONH, SO2NH, NH, CH:N, O] are aldose reductase inhibitors. Thus, 2-F3COC6H4CO2H was converted to the Ph ester which was treated with MeNO2 to give 2-F3COC6H4COCH2NO2. This compd. had an IC50 for aldose reductase inhibition of 41 nM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

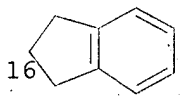
MSTR 1A

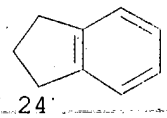
G3—G6—G1
3 5

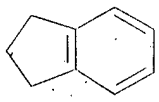
G1 = 212 / (SC naphthyl (SR (1-) G24)) /
(EX benzothienyl (SR (1-) G24) / thienyl (SR (1-) G24))

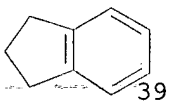
G23—G22
212

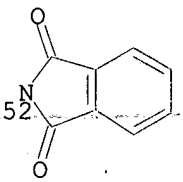
G2 = F / Cl / Br / I / CN / alkyl<(1-7)> / CF3 /
alkoxy<(2-7)> / OCF3
G3 = H / F / Cl / Br / I / trialkylsilyl<(1-7)> /
aryl<EC (6-10) C, RC (1-2)> (SO (1-) G4) /
aryloxy<EC (6-10) C, RC (1-2)> (SO (1-) G4) /
cycloalkyl<(3-12)> (SO (1-) G4) /
Hy<EC (3-10) A (1-4) Q (0-) O (0-) S (0-) N (0) OTHERQ,
RC (1-2)> (SO (1-) G4) / 16 / 24 / 31 / 39 / 52 / 63 / 69 /
77 / 86 / 92 / 98 / 104 / 116

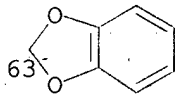


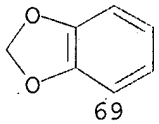


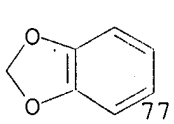


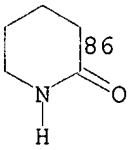


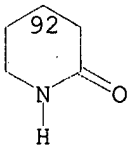


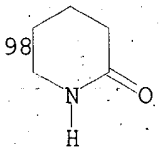


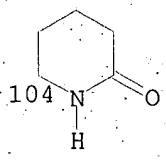


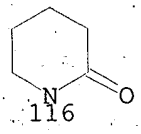




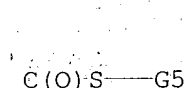






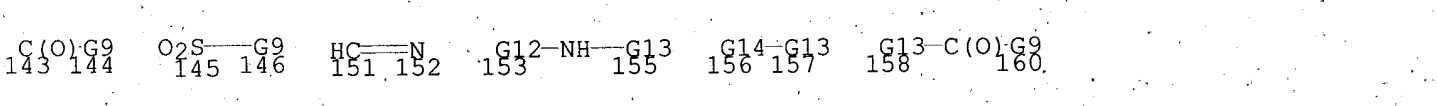


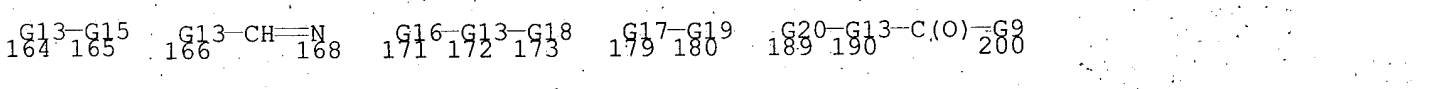
G4 = F / Cl / Br / I / alkyl<(1-7)> / alkoxy<(1-7)> / CF3 / **CO2H** / CONH2 / alkylaminocarbonyl<(1-7)> / dialkylaminocarbonyl<(1-7)> / alkoxycarbonyl<(1-7)> / NH2 / alkylamino<(1-7)> / dialkylamino<(1-7)> / NO2 / CN / OH / OCF3 / cycloalkyl<(3-12)> / SO3H / alkylthio<(1-7)> / alkylsulfinyl<(1-7)> / alkylsulfonyl<(1-7)> / alkylcarbonyl<(1-7)> / 140 / 137 / alkylcarbonylamino<(1-7)> / aryl<EC (6-10) C, RC (1-2)>

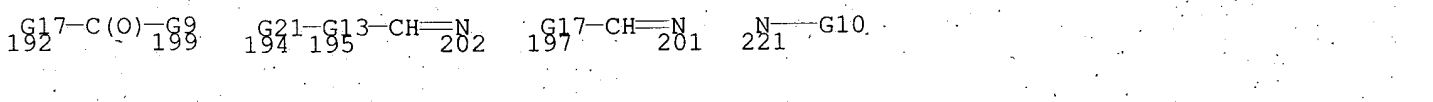


G5 = alkyl<(1-7)>

G6 = 143-3 144-5 / 145-3 146-5 / alkenylene<(2-)> (SO) / S / S(O) / SO2 / G7 / alkylene<EC (1-5) C, DC (0) M3> (SO (1-) G8) / NH / 221 / 151-3 152-5 / O / 153-3 155-5 / 156-3 157-5 / 158-3 160-5 / 164-3 165-5 / 166-3 168-5 / 171-3 173-5 / 179-3 180-5 / 189-3 200-5 / 192-3 199-5 / 194-3 202-5 / 197-3 201-5







G7 = **(1-5) CH2**

G8 = alkyl<(1-7)> / cycloalkyl<(3-12)> / CF3 / alkoxy<(1-7)>

G9 = NH / 147

G10 = alkyl<(1-7)> / aryl<EC (6-10) C, RC (1-2)> / Hy<EC (3-10) A (1-4) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> / 149

G11 = H / alkyl<(1-7)> / aryl<EC (6-10) C, RC (1-2)> /

Hy<EC (3-10) A (1-4) Q (0-) O (0-) S (0-) N (0) OTHERQ,
RC (1-2)>
G12 = C(O) / SO2
G13 = alkylene<EC (1-5) C, DC (0) M3> (SR) / G7
G14 = S / S(O) / SO2
G15 = NH / O / 169 / 162-164 163-5

O_2S—G9 (162 163) N—G10 (169)

G16 = 174-3 175-172 / 176-3 177-172 / S / S(O) / SO2

O_2S—NH (174 175) C(O)NH (176 177)

G17 = alkenylene<(2-)> (SO)
G18 = 181-172 182-5 / NH / 185 / O

O_2S—G9 (181 182) N—G10 (185)

G19 = 183-179 184-5 / NH / 187 / O

O_2S—G9 (183 184) N—G10 (187)

G20 = 203-3 204-190 / 205-3 206-190 / S / S(O) / SO2

O_2S—NH (203 204) C(O)NH (205 206)

G21 = 207-3 208-195 / 209-3 210-195 / S / S(O) / SO2

O_2S—NH (207 208) C(O)NH (209 210)

G22 = 6 / **219**

C(O)CH_2—NO_2 (6) C(O)G25 (219)

G23 = arylene<EC (6-10) C, RC (1-2)> (SO G2) /
Hy<EC (3-10) A (1-4) Q (0-) O (0-) S (0-) N (0) OTHERQ,
RC (1-2)> (SO G2) / **(SC phenylene (SO G2))**
G24 = 214 / 217 / R

C(O)CH_2—NO_2 (214) C(O)G25 (217)

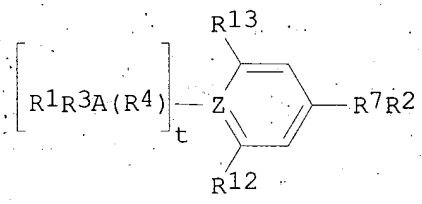
G25 = **OH** / OPh
DER: and addition salts with pharmaceutically acceptable bases
MPL: claim 1
NTE: substitution is restricted
NTE: additional ring formation also claimed
NTE: also incorporates claims 11 and 12

L3 ANSWER 28 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:198001 MARPAT
TITLE: Heart disease treatment agents containing aromatic compounds
INVENTOR(S): Taninaka, Mikio; Nishishima, Fuyuhiko; Kanno, Mikio; Takahashi, Hiroshi; Suzuki, Shigeru; Enari, Hiroyuki; Ise, Michihito
PATENT ASSIGNEE(S): Kureha Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10203981	A2	19980804	JP 1997-20925	19970121
CA 2224910	AA	19980721	CA 1997-2224910	19971216
US 5932575	A	19990803	US 1997-991411	19971216
AU 9850394	A1	19980723	AU 1998-50394	19980108
AU 714013	B2	19991216		
EP 864568	A1	19980916	EP 1998-100888	19980120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6211175	B1	20010403	US 1998-166759	19981006

PRIORITY APPLN. INFO.: JP 1997-20925 19970121
US 1997-991411 19971216

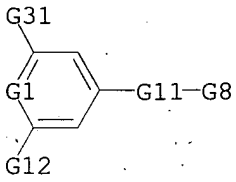
GI



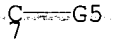
I

AB The title agents contain arom. compds. I [R1 = H, C1-8 (halo)alkyl, NH2, NHR21; R2 = OH, OR22, (substituted) 3- to 7-membered satd. aliph. cycloamino, (substituted) N-contg. 3- to 7-membered satd. aliph. cycloalkyl, NHR23, N(R24)2, NH2; R4 = H, C1-8 alkyl, COR25; R7 = CO, SO2; R8 = CO, single bond; R12 = R11-R5; R11 = NR5, NH, O, NR26, NCOR27, NCONH2, NCONHR28; R5 = H, substituted benzyl; R13 = H, C1-6 (halo)alkyl, NHCO(CH2)mPh, NHCOR29, NHCOCHPh2, NH2, NHR30, (CH2)nPh; Z = C, CH, N; A = CH, N; R21-R30 = C1-8 (halo)alkyl; m, n = 0-6; t = 0, 1] or their pharmacol. acceptable salts as active ingredients. Chlorination of 300 mg 3-N-[[(4-carboxyphenyl)methyl]valeramido]-4-dimethylaminobenzoic acid morpholide with SOCl2 followed by esterification with 2-dimethylaminoethanol gave 288 mg 4-dimethylamino-3-N-[[[4-(2'-dimethylaminoethoxycarbonyl)phenyl]methyl]valeramido]benzoic acid morpholide (II). Administration of II at 20 mg/kg p.o. for 4 wk decreased heart wt. in rats with cardiac hypertrophy. II showed substantially no antagonistic activities against angiotensin II receptors (AT1 and AT2) nor antihypertensive effects. II (at 500 mg/kg p.o.) showed no acute toxicity in mice.

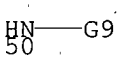
MSTR 1



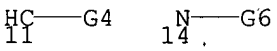
G1 = **7** / N



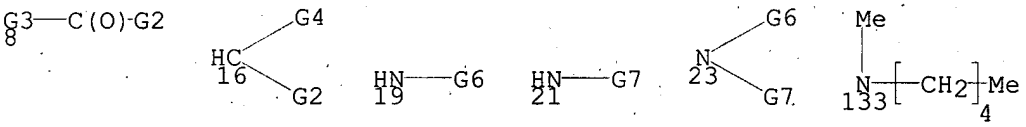
G2 = H / alkyl<(1-8)> (SO (1-) X) / NH2 / 50



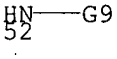
G3 = 11 / NH / 14



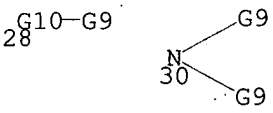
G4 = H / alkyl<(1-8)> / alkylcarbonyl<(1-8)> (SO (1-) X)
G5 = 8 / 16 / NH2 / 19 / 21 / 23 / H / (EX NMe2 / 133 / hexyl / NEt2)



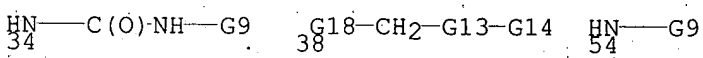
G6 = alkyl<(1-8)> / alkylcarbonyl<(1-8)> (SO (1-) X)
G7 = alkyl<(1-8)> (SO (1-) X) / NH2 / 52



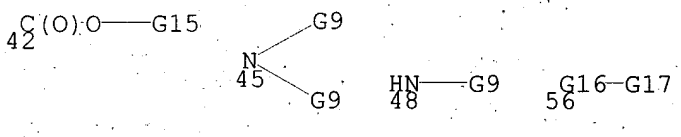
G8 = **OH** / 28 / Hy<EC (1-) Q (1-) N (0-) O (0-) S (0) OTHERQ, AR (0), BD (ALL) SE, RC (1), RS (1) X7> (SO (1-) G9) / 30 / NH2 / (EX morpholino)



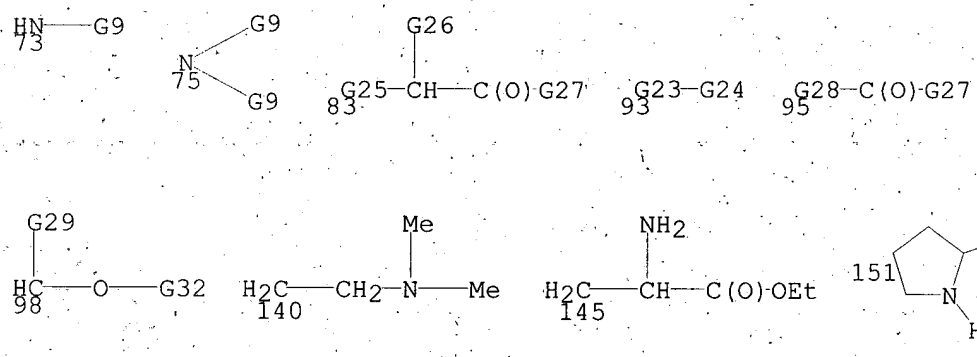
G9 = alkyl<(1-8)> (SO (1-) X)
G10 = O / NH
G11 = **C(O)** / SO2
G12 = NH2 / OH / 54 / alkylcarbonylamino<(1-8)> (SO (1-) X) / NHCONH2 / 34 / **38**



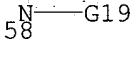
G13 = **phenylene**
G14 = **CO2H** / 42 / OH / alkoxy<(1-8)> (SO (1-) X) / NH2 / 45 / Hy<EC (1-) Q (1-) N (0) OTHERQ, AR (1-), BD (2) D, RC (1), RS (1) E5> / 48 / 56 / (EX tetrazolyl)



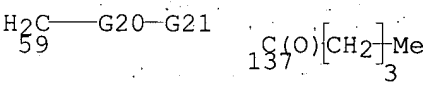
G15 = alkyl<(1-8)> (SO (1-) X) / NH2 / 73 / 75 / Hy<EC (1-) Q (1-) N (0-) O (0-) S (0) OTHERQ, AR (0), BD (ALL) SE, RC (1), RS (1) X7> (SO (1-) G9) / Hy<BD (1-) D, RC (1), RS (1) X7> / 93 / 83 / 95 / 98 / (EX 140 / 145 / 151 / Me)



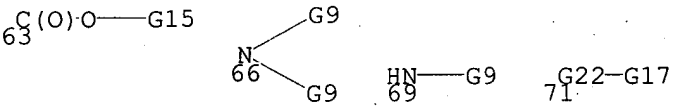
G16 = phenylene
G17 = Hy<EC (1-) Q (1-) N (0) OTHERQ, AR (1-), BD (2) D, RC (1), RS (1) E5> / CO2H
G18 = NH / 58 / **O**



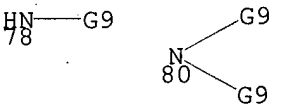
G19 = 59 / alkyl<(1-8)> (SO (1-) X) / alkylcarbonyl<(1-8)> (SO (1-) X) / CONH2 / alkylaminocarbonyl<(1-8)> (SO (1-) X) / (EX 137)



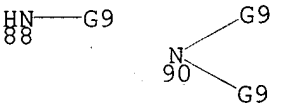
G20 = phenylene
G21 = CO2H / 63 / OH / alkoxy<(1-8)> (SO (1-) X) / NH2 / 66 / Hy<EC (1-) Q (1-) N (0) OTHERQ, AR (1-), BD (2) D, RC (1), RS (1) E5> / 69 / 71 / (EX tetrazolyl)



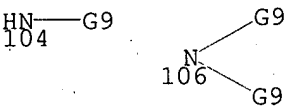
G22 = phenylene
G23 = (1-6) CH2
G24 = NH2 / 78 / 80 / Hy<EC (1-) Q (1-) N (0-) O (0-) S (0) OTHERQ, AR (0), BD (ALL) SE, RC (1), RS (1) X7> (SO (1-) G9) / Hy<BD (1-) D, RC (1), RS (1) X7>



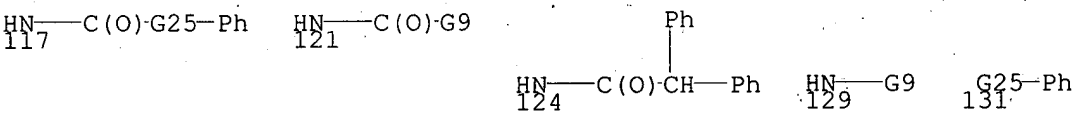
G25 = (0-6) CH2
G26 = NH2 / 88 / 90



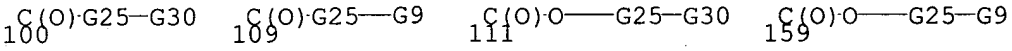
G27 = OH / alkoxy<(1-8)> (SO (1-) X)
G28 = Hy<EC (1-) Q (1-) N, AR (0), BD (ALL) SE, RC (1), RS (1) X6> (SO (1-) G9)
G29 = H / alkyl<(1-8)> (SO (1-) X)
G30 = H / NH2 / 104 / 106 / cycloalkyl<(3-8)>



G31 = H / alkyl<(1-6)> (SO (1-) X) / 117 / 121 / 124 / NH2 / 129 / 131 / (EX Me / CF3)



G32 = 100 / 109 / 111 / 159



MPL: claim 1
NTE: substitution is restricted

L3 ANSWER 29 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:128034 MARPAT
TITLE: Preparation of heterocyclyl-containing O-substituted alcoholamines as fibrinogen receptor antagonist

Searched by Barb O'Bryen, STIC 308-4291

prodrugs

INVENTOR(S): Young, Steven D.; Hartman, George D.; Libby, Laura A.; Egbertson, Melissa S.; Slaughter, Donald E.

PATENT ASSIGNEE(S): Hartman, George D., USA; Libby, Laura A.; Egbertson, Melissa S.; Slaughter, Donald E.; Merck + Co., Inc.; Young, Steven D.

SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800401	A1	19980108	WO 1997-US11047	19970625
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2257950	AA	19980108	CA 1997-2257950	19970625
AU 9735037	A1	19980121	AU 1997-35037	19970625
AU 719102	B2	20000504		
EP 912513	A1	19990506	EP 1997-931401	19970625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000513375	T2	20001010	JP 1998-504266	19970625
US 5932582	A	19990803	US 1997-883107	19970626
PRIORITY APPLN. INFO.:			US 1996-20877P	19960628
			GB 1996-17899	19960828
			WO 1997-US11047	19970625

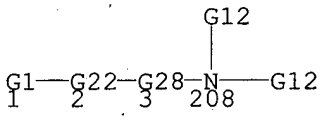
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

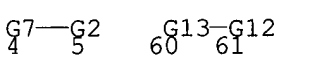
AB The title compds. X-W-Y-Z-(A)r-B [I; W = (CH2)q (wherein q = 0 or 2); X = (un)substituted 5-7 membered (non)arom. ring having 1-3 heteroatoms selected from N, O, and S, 9-10 membered fused (non)arom. ring having 1-3 heteroatoms selected form N, O, and S; Y = (un)substituted 5-6 membered (non)arom. ring having 0-3 heteroatoms selected from N, O, and S, .delta.-lactam, II; XY = III, IV, V (q = 0); Z = (CH2)2, CH:CH, CH2O, etc.; A = (un)substituted 5-6 membered arom. ring having 0-3 heteroatoms selected from N, O, and S, 9-10 membered fused arom. ring having 0-3 heteroatoms selected from N, O, and S; r = 0-1; B = O(CH2)pCH2NR8R7, CH2(CH2)tCH2NR8R7, CH(R9)(CH2)tCH2NR8R7, CH2CH(OPh)CH2NR8R7 (wherein R7-R9 = H, halo, C1-10 alkyl, etc.; p = 1-4; t = 0-4)], useful in inhibiting the binding of fibrinogen to blood platelets, inhibiting the aggregation of blood platelets, treating or preventing thrombus or embolus formation, inhibiting osteoclast mediated bone resorption, inhibiting angiogenesis, and inhibiting tumor growth, were prepd. and formulated. Thus, reaction of 4-[4-(1,1-dimethylethoxycarbonyl)piperazin-1-yl]benzoic acid with 1-(1,1-dimethylethoxycarbonylamino)-2-(4-amino-3-methylphenoxy)ethane in the presence of chloro-N,N,N',N'-bis(pentamethylene)formamidinium hexafluorophosphate and (iPr)2NEt in CH2Cl2 followed by deprotection of the intermediate afforded the title compd. VI.2HCl. Compds. I are prodrugs of active acids X-W-Y-Z-(A)r-B [B = O(CH2)pCO2H, CH2(CH2)tCO2H, CH(R9)(CH2)tCO2H, CH2CH(OPh)CO2H] which have been evaluated in vitro and found to have an IC50 for inhibiting platelet aggregation of between 8 nM

and 10 .mu.M. Compds. I are effective at 0.9 mg/day - 1.8 g/day when administered orally to a typical 90 kg patient.

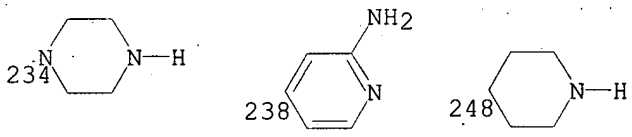
MSTR 1A



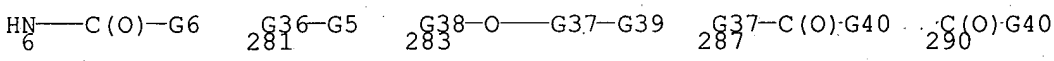
G1 = 4 / 60

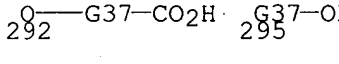


G2 = Hy<EC (5-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO (1-2) G3) / (SC 234 / 238 / 248)



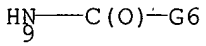
G3 = F / Cl / Br / I / alkyl<(1-10)> / cycloalkyl<(3-8)> / Ph (SO (1-) G4) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1)> (SO (1-) G4) / 281 / NH2 / 6 / alkylamino<(1-6)> / dialkylamino<(1-6)> / 283 / 287 / **290** / 292 / OH / 295





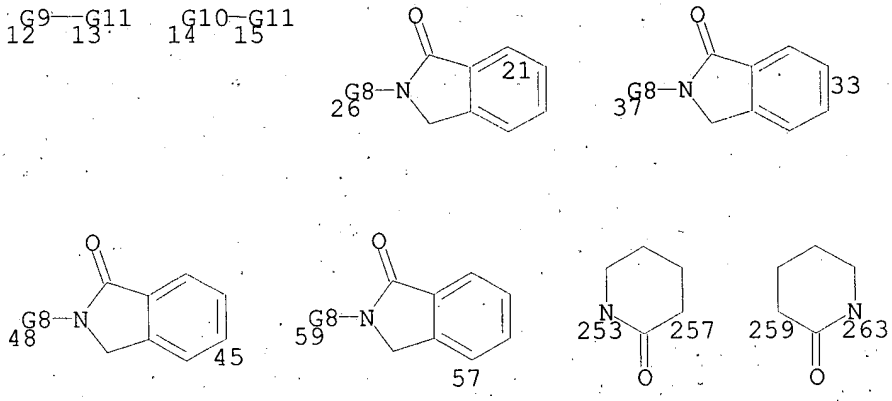
G4 = NH2 / F / Cl / Br / I

G5 = Ph (SO (1-) G4) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1)> (SO (1-) G4) / NH2 / 9 / alkylamino<(1-6)> / dialkylamino<(1-6)>

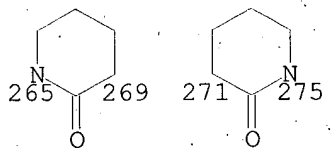


G6 = H / Ak<(1-2)>

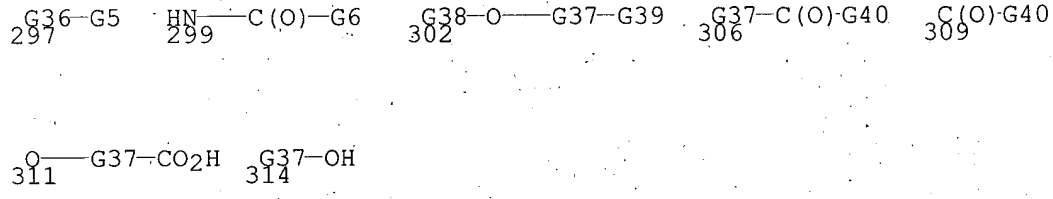
G7 = **Cy<EC (0-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X6> (SO (1) G3)** / 12-2 13-5 / R<TX ".delta.-lactam"> / 14-2 15-5 / 21-2 26-5 / 33-2 37-5 / 45-2 48-5 / 57-2 59-5 / (SC p-C6H4 / 253-2 257-5 / 259-2 263-5)



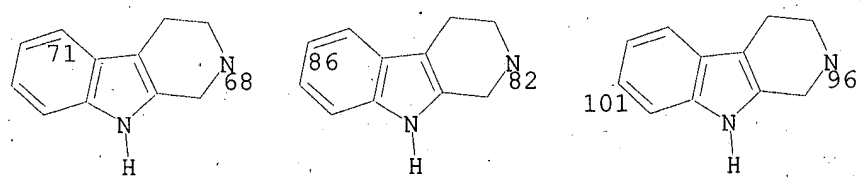
G8 = (0-2) CH2
G9 = Cy<EC (0-3) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RC (1), RS (1) M5 (1) X6> (SO (1) G3) / (SC p-C6H4)
G10 = R<TX ".delta.-lactam"> / (SC 265-15 269-2 /
271-15 275-2)

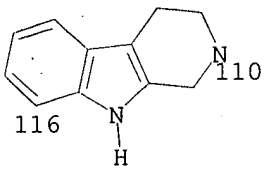


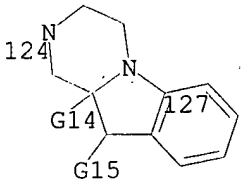
G11 = (1-2) CH2
G12 = H / F / Cl / Br / I / alkyl<(1-10)> /
cycloalkyl<(3-8)> / Ph (SO (1-) G4) /
heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RC (1)> (SO (1-) G4) / 297 / NH2 / 299 / alkylamino<(1-6)> /
dialkylamino<(1-6)> / 302 / 306 / 309 / 311 / OH / 314

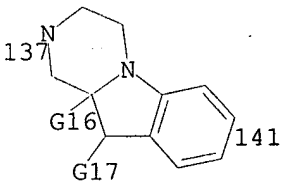


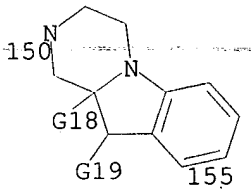
G13 = 71-2 68-61 / 86-2 82-61 / 101-2 96-61 /
116-2 110-61 / 127-2 124-61 / 141-2 137-61 / 155-2 150-61 /
169-2 163-61

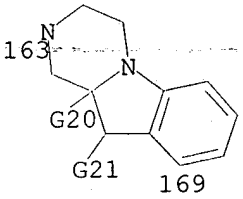




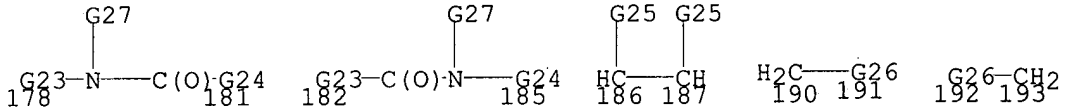


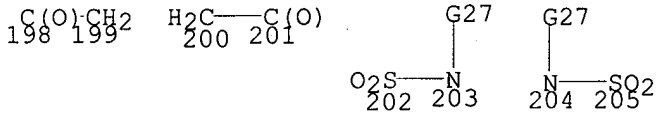




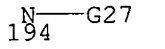


G14 = H
G15 = H
G16 = H
G17 = H
G18 = H
G19 = H
G20 = H
G21 = H
G22 = 178-1 181-3 / 182-1 185-3 / 186-1 187-3 / CH=CH /
190-1 191-3 / 192-1 193-3 / 198-1 199-3 / 200-1 201-3 /
202-1 203-3 / 204-1 205-3

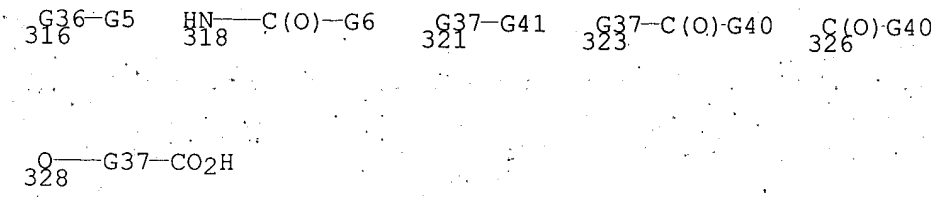




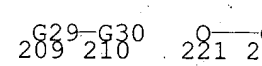
G23 = (0-4) CH2
G24 = (0-6) CH2
G25 = H / (-1) OH
G26 = **O** / 194



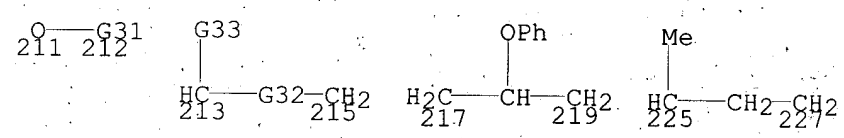
G27 = H / F / Cl / Br / I / alkyl<(1-10)> /
cycloalkyl<(3-8)> / Ph (SO (1-) G4) /
heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RC (1)> (SO (1-) G4) / 316 / NH2 / 318 / alkylamino<(1-6)> /
dialkylamino<(1-6)> / alkoxy<(1-4)> / 321 / 326 / 323 / 328 /
OH



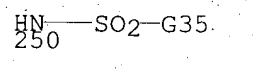
G28 = 221-2 222-208 / 209-2 210-208



G29 = **Cy<EC (5-10) A (0-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO (1-3) G3) /** (SC phenylene (SO (1-3) G34))
G30 = 211-209 212-208 / 213-209 215-208 / 217-209 219-208 / (SC 225-209 227-208)



G31 = (2-5) CH2
G32 = (0-4) CH2
G33 = H / R
G34 = F / Cl / Br / I / alkyl<(1-3)> / 250 / Me



G35 = alkyl<(1-3)> / Me
G36 = alkylene<(1-8)>
G37 = alkylene<(1-6)>
G38 = NULL / alkylene<(1-6)>
G39 = H / Ph (SO (1-) G4) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1)> (SO (1-) G4)
G40 = **OH** / alkoxy<(1-3)>
G41 = OH / alkoxy<(1-4)>
G14+G15= NULL
G16+G17= NULL
G18+G19= NULL
G20+G21= NULL
DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: additional ring formation also claimed

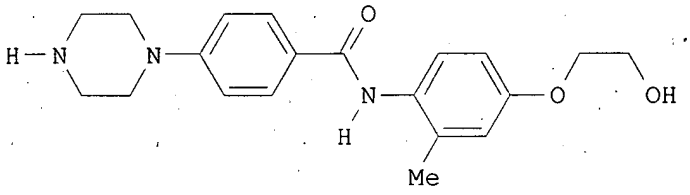
L3 ANSWER 30 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:128033 MARPAT
TITLE: Preparation of N-(2-hydroxyethoxy)phenyl heterocyclyl-containing amides as fibrinogen receptor antagonist prodrugs
INVENTOR(S): Egbertson, Melissa S.; Hartman, George D.; Lumma, William C.; Wai, John S.; Young, Steven D.
PATENT ASSIGNEE(S): Merck + Co., Inc., USA; Egbertson, Melissa S.; Hartman, George D.; Lumma, William C.; Wai, John S.;

Searched by Barb O'Bryen, STIC 308-4291

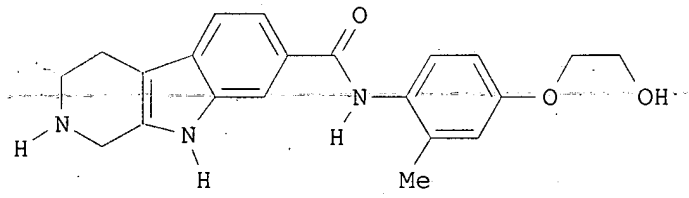
Young, Steven D.
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800144	A1	19980108	WO 1997-US11037	19970625
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2257937	AA	19980108	CA 1997-2257937	19970625
AU 9735033	A1	19980121	AU 1997-35033	19970625
AU 709631	B2	19990902		
EP 912182	A1	19990506	EP 1997-931396	19970625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000514427	T2	20001031	JP 1998-504262	19970625
US 5990107	A	19991123	US 1997-883114	19970626
PRIORITY APPLN. INFO.:			US 1996-20976P	19960628
			GB 1996-17983	19960828
			WO 1997-US11037	19970625

GI



II



III

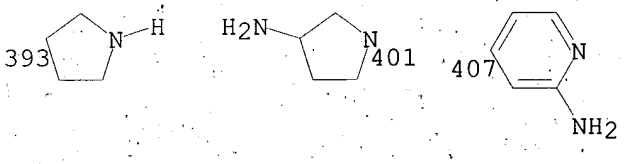
AB The title compds. having the structure, for example, of formula X-Y-C(O)NH-A-OCH2CH2OH [I; X = 6-membered arom. or nonarom. ring having 1-3 N atoms; Y = 6-membered arom. or nonarom. ring having 0-3 N atoms; A = (un)substituted 6-membered arom. ring] more particularly, formulas II.HCl and III, were prepd. and formulated. Thus, reaction of 2-(1,1-dimethylethoxycarbonyl)-1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-7-carboxylic acid with 2-(3-methyl-4-aminophenoxy)ethanol.HCl in the presence of (iPr)2NH and PYCLU in CH2Cl2 followed by treatment of the Boc-protected product with HCl gas in dioxane afforded III. Compds. I are

prodrugs of active acids X-Y-C(O)NH-A-OCH2CO2H which have been evaluated in vitro and found to have an IC50 of 0.008-2 .mu.M for inhibiting platelet aggregation. Compds. I are effective at 0.9 mg/day - 1.8 g/day (when administered to 90 kg patient)..

MSTR 2

G7—G13—G18—G21—CH_2—C(O)—G22
19 3 4 5 201

G1 = Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-) G2) / (SC piperazino / 4-pyridyl / 393 / 401 / 407)



G2 = F / Cl / Br / I / alkyl<(1-10)> / cycloalkyl<(3-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO) / NH2 / alkyl<(1-8)> (SR (1-) G5) / 6 / 475 / 8 / alkylamino<(1-6)> / dialkylamino<(1-6)> / alkoxy<(1-6)> (SO (1-) G5) / CO2H / alkoxycarbonyl<(1-3)> / alkoxy<(1-6)> (SR CO2H) / OH

G3—G4 HN—C(O)-G6 G33—G34
6 8 475

G3 = alkylene<(1-8)>
G4 = NH2 / 11 / alkylamino<(1-6)> / dialkylamino<(1-6)>

HN—C(O)-G6
11

G5 = Cb<EC (6) C, AR (1-), BD (ALL) N, RC (1), RS (1) E6> (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO)
G6 = H / alkyl<(1-3)>
G7 = 2 / 20

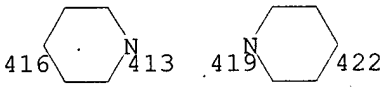
G1—G9 G10—G11
1 2 20 21

G8 = F / Cl / Br / I / alkyl<(1-10)> / cycloalkyl<(3-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO) / NH2 / alkyl<(1-8)> (SR (1-) G5) / 14 / 477 / 16 / alkylamino<(1-6)> / dialkylamino<(1-6)> / alkoxy<(1-6)> (SO (1-) G5) / **CO2H** / alkoxycarbonyl<(1-3)> / alkoxy<(1-6)> (SR CO2H) / OH

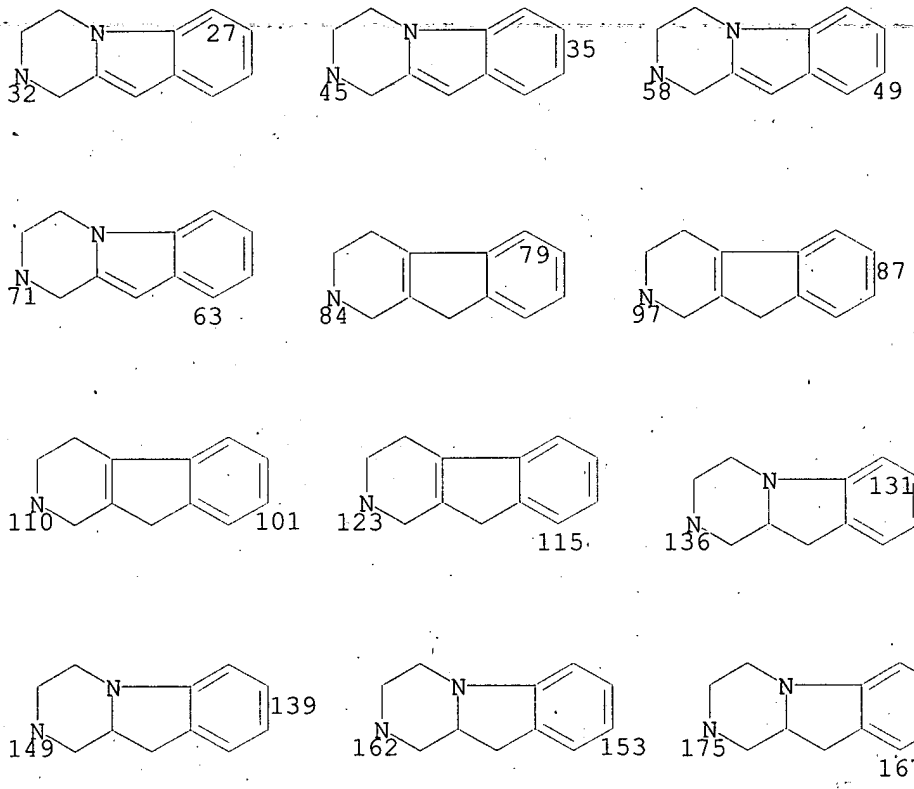
G3—G4 HN—C(O)-G6 G33—G34
14 16 477

G9 = Hy<EC (5-6) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1)> (SO (1-) G8) / phenylene (SO (1-) G36) /

Cb<EC (5-6) C, AR (0)> (SO (1-) G8) / (SC 416-1 413-3 / 419-1 422-3)



G10 = 27-3 32-21 / 35-3 45-21 / 49-3 58-21 / 63-3 71-21 / 79-3 84-21 / 87-3 97-21 / 101-3 110-21 / 115-3 123-21 / 131-3 136-21 / 139-3 149-21 / 153-3 162-21 / 167-3 175-21



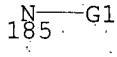
G11 = H / F / Cl / Br / I / alkyl<(1-10)> / cycloalkyl<(3-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO) / NH2 / alkyl<(1-6)> (SR (1-) G5) / 178 / 479 / 180 / alkylamino<(1-6)> / alkoxy<(1-6)> (SO (1-) G5) / CO2H / alkoxycarbonyl<(1-3)> / alkoxy<(1-6)> (SR CO2H) / OH

G3—G4 HN——C(O)-G6 G33—G34
178 180 479

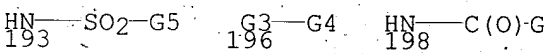
G13 = 183-19 184-4 / 188-19 187-4 / CH2CH2 / CH=CH / **189-19 190-4** / 192-19 191-4 / NULL

G16—G14 G14—G16 H2C——G17 G17—CH2
183 184 188 187 189 190 192 191

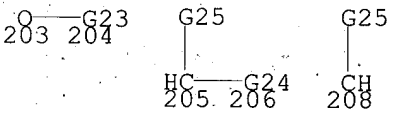
G14 = NH / 185



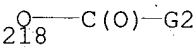
G15 = R / (SC Me)
G16 = C(O) / CH2
G17 = O / C(O) / CHOH
G18 = **Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-) G19)** / phenylene (SO G35) / Cb<EC (5-10) C, RC (1-2)> (SO (1-) G19)
G19 = F / Cl / Br / I / alkyl<(1-10)> / cycloalkyl<(3-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO) / NH2 / alkyl<(1-6)> (SR (1-) G5) / 193 / 196 / 481 / 198 / alkylamino<(1-6)> / dialkylamino<(1-6)> / alkoxy<(1-6)> (SO (1-) G5) / **CO2H** / alkoxycarbonyl<(1-3)> / alkoxy<(1-6)> (SR CO2H) / OH / (SC CF3 / Me / OMe)



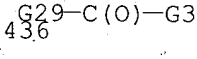
G21 = 203-4 204-201 / CH2 / CH2CH2 / CH2CH2CH2 / 205-4 206-201 / 208



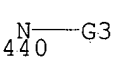
G22 = OH / 218



G23 = (1-2) CH2
G24 = (1-2) CH2
G25 = H / R / alkyl<(1-10)> (SO) / (SC Me)
G26 = alkyl<(1-8)> / cycloalkyl<(3-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO) / alkyl<(1-3)> (SR (1-) G5) / (SC 436 / Et)



G29 = (1-3) CH2
G30 = NH / 440



G31 = Me / Et / Pr-n
G33 = alkylene<(1-6)>
G34 = alkoxy<(1-6)> / alkoxy<(1-6)> (SR (1-) G5) / CO2H / alkoxycarbonyl<(1-3)> / OH
G35 = R / (SC NHSO2Ph / Me / OMe / CF3 / Cl / NO2 / Br)
G36 = R / (SC Me / NHSO2Me / Br)
DER: and pharmaceutically acceptable salts
MPL: claim 1

L3 ANSWER 31 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:128032 MARPAT
TITLE: Preparation of heterocyclyl-substituted phenoxyalkanoic acids as fibrinogen receptor antagonists
INVENTOR(S): Duggan, Mark E.; Egbertson, Melissa S.; Hartman, George D.; Young, Steven D.; Ihle, Nathan C.
PATENT ASSIGNEE(S): Merck + Co., Inc., USA; Duggan, Mark E.; Egbertson, Melissa S.; Hartman, George D.; Young, Steven D.; Ihle, Nathan C.
SOURCE: PCT Int. Appl., 270 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800134	A1	19980108	WO 1997-US11133	19970625
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2258093	AA	19980108	CA 1997-2258093	19970625
AU 9735798	A1	19980121	AU 1997-35798	19970625
AU 721130	B2	20000622		
EP 912175	A1	19990506	EP 1997-932307	19970625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000514061	T2	20001024	JP 1998-504291	19970625

PRIORITY APPLN. INFO.: US 1996-20975P 19960628
GB 1997-893 19970117
WO 1997-US11133 19970625

GI

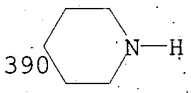
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

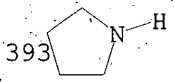
AB The title compds. X-Y-Z-A-B [I; X = (un)substituted 5-7- membered arom. or nonarom. ring, having 1-3 heteroatoms selected from N, O, and S, (un)substituted 9-10 membered fused arom. or nonarom. ring, having 1-3 heteroatoms selected from N, O, and S; Y = (un)substituted 5-6 membered arom. or nonarom. ring, having 0-3 heteroatoms selected from N, O, and S; XY = II, III, IV, V; Z = C(O)NR4, N(R4)C(O), CH2CH2, CH:CH, etc.; R4 = H, C1-4 alkyl, C3-6 cycloalkyl; A = (un)substituted 5-6 membered arom. ring, having 0-3 heteroatoms selected from N, O, and S, 9-10 membered fused arom. ring having 0-3 heteroatoms (N, O, and S); B = C(CH2)mCO2R9, (CH2)nCO2R9, CH(R8)(CH2)pCO2R9, OCH(R8)(CH2)pCO2R9 (wherein m = 1-3; n = 0-3; p = 0-3; R8 = H, aryl, amino, etc.; R9 = H, aryl, C1-8 alkyl, etc.)], useful in inhibiting the binding of fibrinogen to blood platelets, inhibiting the aggregation of blood platelets, treating thrombus or embolus formation, inhibiting osteoclast mediated bone resorption, inhibiting angiogenesis, and in inhibiting tumor growth, were prepd. and formulated. Thus, a few-step detailed synthesis of the acid VI which showed IC50 in the range between 10 nM and 50 mM against ADP-stimulated platelet aggregation, was described.

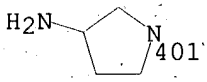
MSTR 1A

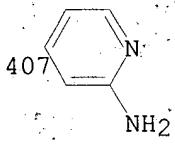
G7—G13—G18—G21—C(O)—G22
19 3 4 5 201

G1 = Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-) G2) / (SC piperazino / 390 / 4-pyridyl / 393 / 401 / 407)









G2 = F / Cl / Br / I / alkyl<(1-10)> / cycloalkyl<(3-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO) / NH2 / alkyl<(1-8)> (SR (1-) G5) / 6 / 475 / 8 / alkylamino<(1-6)> / alkoxy<(1-6)> (SO (1-) G5) / CO2H / alkoxycarbonyl<(1-3)> / alkoxy<(1-6)> (SR CO2H) / OH

G3—G4 HN——C(O)G6 G33—G34
6 8 475

G3 = alkylene<(1-8)>
G4 = NH2 / 11 / alkylamino<(1-6)> / dialkylamino<(1-6)>

HN——C(O)G6
11

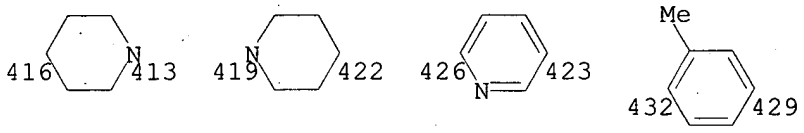
G5 = Cb<EC (6) C, AR (1-), BD (ALL) N, RC (1), RS (1) E6> (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO)
G6 = H / alkyl<(1-3)>
G7 = 2 / 20

G1—G9 G10—G11
1 2 20 21

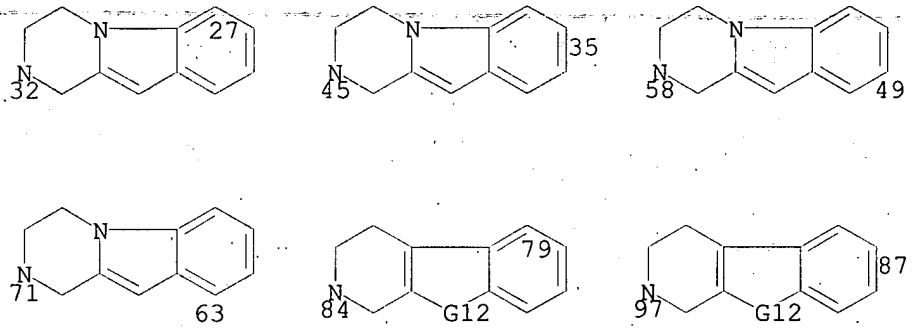
G8 = F / Cl / Br / I / alkyl<(1-10)> / cycloalkyl<(3-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO) / NH2 / alkyl<(1-8)> (SR (1-) G5) / 14 / 477 / 16 / alkylamino<(1-6)> / dialkylamino<(1-6)> / alkoxy<(1-6)> (SO (1-) G5) / **CO2H** / alkoxycarbonyl<(1-3)> / alkoxy<(1-6)> (SR CO2H) / OH / (SC Me)

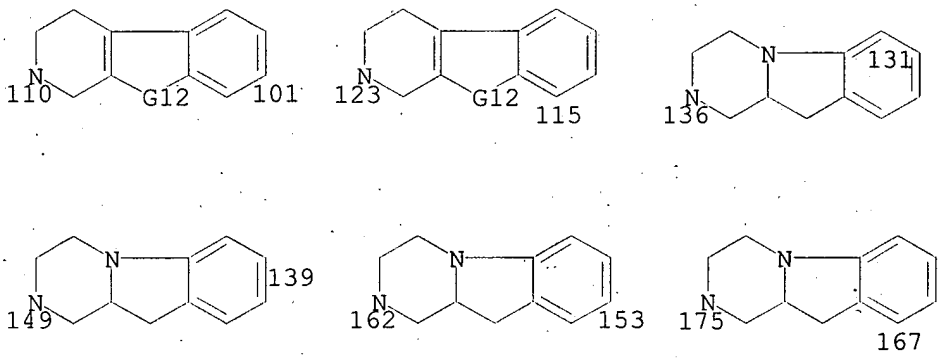
G3—G4 HN——C(O)G6 G33—G34
14 16 477

G9 = Hy<EC (5-6) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1)> (SO (1-) G8) / phenylene (SO) / **Cb<EC (5-6) C, AR (0)> (SO (1-) G8)** / (SC 416-1 413-3 / 419-1 422-3 / 426-1 423-3 / 432-1 429-3)



G10 = 27-3 32-21 / 35-3 45-21 / 49-3 58-21 / 63-3 71-21 /
79-3 84-21 / 87-3 97-21 / 101-3 110-21 / 115-3 123-21 /
131-3 136-21 / 139-3 149-21 / 153-3 162-21 / 167-3 175-21





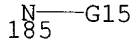
G11 = H / F / Cl / Br / I / alkyl<(1-10)> /
cycloalkyl<(3-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)>
(SO) / NH2 / alkyl<(1-6)> (SR (1-) G5) / 178 / 479 / 180 /
alkylamino<(1-6)> / alkoxy<(1-6)> (SO (1-) G5) / CO2H /
alkoxycarbonyl<(1-3)> / alkoxy<(1-6)> (SR CO2H) / OH

G3—G4 HN——C(O)G6 G33—G34
178 180 479

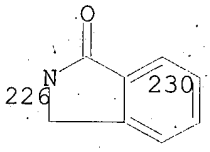
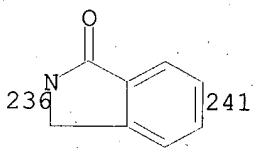
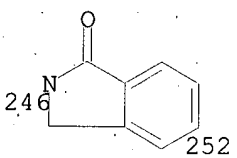
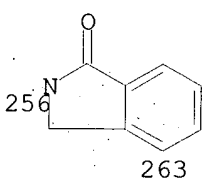
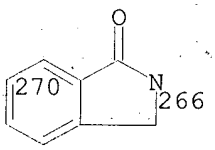
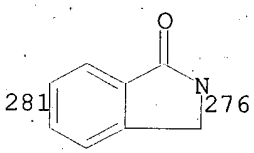
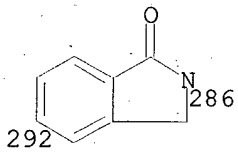
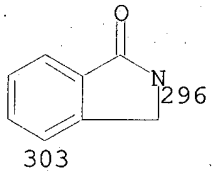
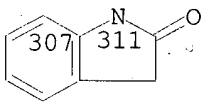
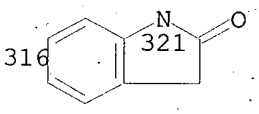
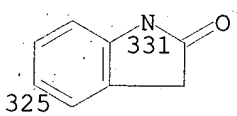
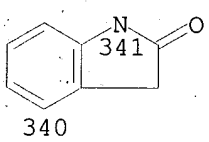
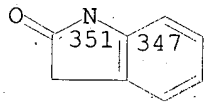
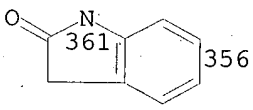
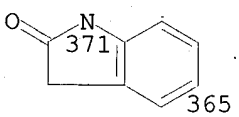
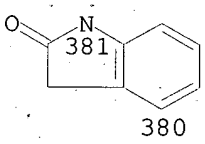
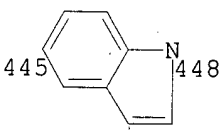
G12 = NH / O
G13 = 183-19 184-4 / 188-19 187-4 / CH2CH2 / CH=CH /
189-19 190-4 / 192-19 191-4

G16—G14 G14—G16 H2C——G17 G17—CH2
183 184 188 187 189 190 192 191

G14 = NH / 185

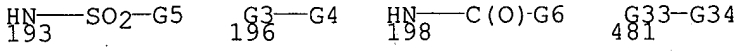


G15 = alkyl<(1-4)> / cycloalkyl<(3-6)> / (SC Me)
G16 = C(O) / CH2
G17 = **O** / C(O) / CHOH
G18 = Hy<EC (5-10) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-) G19) / **phenylene (SO G35)** / Cb<EC (5-10) C, RC (1-2)> (SO (1-) G19) / (SC 226-3 230-5 / 236-3 241-5 / 246-3 252-5 / 256-3 263-5 / 270-3 266-5 / 281-3 276-5 / 292-3 286-5 / 303-3 296-5 / 307-3 311-5 / 316-3 321-5 / 325-3 331-5 / 340-3 341-5 / 351-3 347-5 / 361-3 356-5 / 371-3 365-5 / 381-3 380-5 / 445-3 448-5)

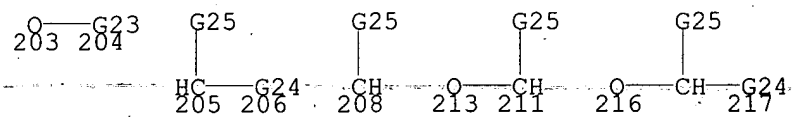


















G19 = F / Cl / Br / I / alkyl<(1-10)> / cycloalkyl<(3-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO) / NH2 / alkyl<(1-6)> (SR (1-) G5) / 193 / 196 / 481 / NO2 / alkylsulfonylamino<(1-3)> / alkyl (SR (3) G20) / 198 / alkylamino<(1-6)> / dialkylamino<(1-6)> / alkoxy<(1-6)> (SO (1-) G5) / CO2H / alkoxycarbonyl<(1-3)> /

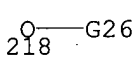
alkoxy<(1-6)> (SR CO2H) / OH / (SC CF3 / Me / OMe)



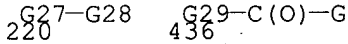
G20 = F / Cl / Br / I
G21 = 203-4 204-201 / NULL / CH2 / CH2CH2 / CH2CH2CH2 / 205-4 206-201 / 208 / 213-4 211-201 / 216-4 217-201



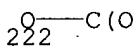
G22 = **OH** / 218



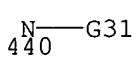
G23 = (1-3) CH2
G24 = (1-3) CH2
G25 = H / R / alkyl<(1-10)> (SO) / (SC Me)
G26 = alkyl<(1-8)> / Ph (SO) / heteroaryl<EC (5-6) A, RC (1)> (SO) / alkyl<(1-6)> (SR (1-) G5) / 220 / (SC 436 / Et)



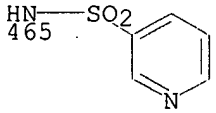
G27 = alkylene<(1-6)>
G28 = alkylcarbonyloxy<(1-8)> / 222 / alkylcarbonyloxy<(1-6)> (SR (1-) G5) / alkylaminocarbonyl<(1-8)> / dialkylaminocarbonyl<(1-8)>



G29 = (1-3) CH2
G30 = NH / 440



G31 = Me / Et / Pr-n
G33 = alkylene<(1-6)>
G34 = alkoxy<(1-6)> / alkoxy<(1-6)> (SR (1-) G5) / CO2H / alkoxycarbonyl<(1-3)> / OH
G35 = R / (SC NHSO2Ph / Me / OMe / CF3 / Cl / NO2 / Br / NHSO2Me / 465)



DER: and pharmaceutically acceptable salts

MPL: claim 1

L3 ANSWER 32 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:346406 MARPAT
TITLE: Preparation of acylaminocinnamates and related compounds as integrin antagonists.
INVENTOR(S): Chen, Barbara B.; Chen, Helen Y.; Clare, Michael; Docter, Stephen H.; Khanna, Ish Kumar; Koszyk, Francis Jan; Malecha, James W.; Miyashiro, Julie M.; et al.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA; Chen, Barbara B.; Chen, Helen Y.; Clare, Michael; Docter, Stephen H.; Khanna, Ish Kumar; Koszyk, Francis Jan; Malecha, James W.
SOURCE: PCT Int. Appl., 278 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9736860	A1	19971009	WO 1997-US4462	19970325
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EP 894084	A1	19990203	EP 1997-916111	19970325
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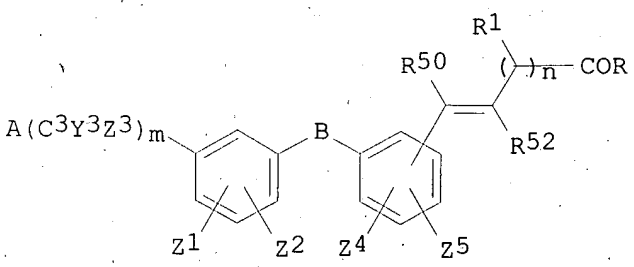
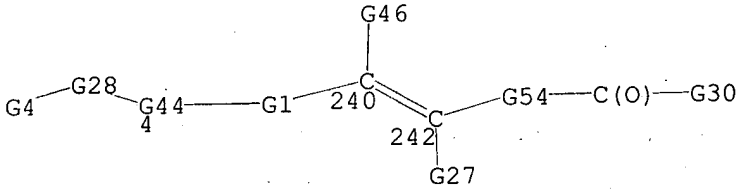


I

AB Title compds. [I; A = NR5C(Y1)NR7R8, NR5C(NR7)Y2; Y1 = NR2, O, S; R = XR3; R1 = H, alkyl, amino, acylamino, etc.; X = O, S, NR4; R2 = H, (substituted) alkyl, aryl, OH, alkoxy, cyano, NO2, amino, aminocarbonyl, alkenyl, alkynyl, etc.; R3, R4 = H, alkyl, alkenyl, alkynyl, haloalkyl, aryl, aralkyl, sugar residue, steroid residue, etc.; R5 = H, alkyl, alkenyl, alkynyl, PhCH2, PhCH2CH2; R7 = H, (substituted) alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, bicycloalkyl, aryl, acyl, etc.; R50 = H, alkyl, (substituted) aryl, etc.; R52 = H, acylamino, (substituted)

hydrazino; R2R7 = (substituted) heterocyclyl, heteroaryl; R7R8 = (substituted) heterocyclyl; Y2R7 = (substituted) heterocyclyl; Z1, Z2, Z3, Z5 = H, alkyl, OH, alkoxy, aryloxy, aralkoxy, halo, haloalkyl, haloalkoxy, NO2, amino, aminoalkyl, cyano, alkylsulfonyl, carboxyalkenyl, (fused) aryl, etc.; B = (CH2)pO, CH:CH, CH2CONH, CONH(CH2)p, CO2, SO2NH, etc.; m = 0-2; n = 0-3; p = 0-2]. Thus, 3-[2-methoxy-4-[[[3-[(1,2,3,4-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]phenyl]propionic acid trifluoroacetate (prepn. given) antagonized .alpha.v.beta.3 with IC50 = 0.43 nM.

MSTR 1



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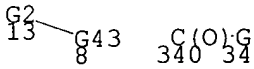
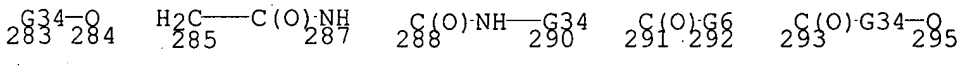
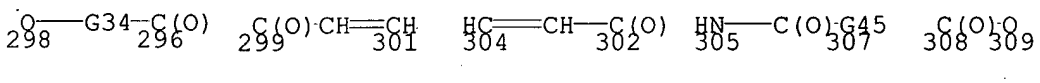
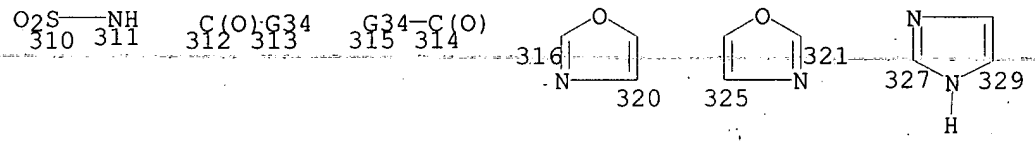
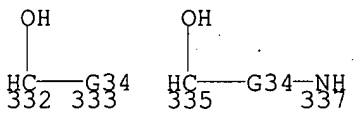


G2 = **283-4 284-8** / CH=CH / 285-4 287-8 / 288-4 290-8 / 291-4 292-8 / 293-4 295-8 / 298-4 296-8 / 299-4 301-8 / 304-4 302-8 / 305-4 307-8 / 308-4 309-8 / 310-4 311-8 / 312-4 313-8 / 315-4 314-8 / 316-4 320-8 / 325-4 321-8 / 327-4 329-8 / 332-4 333-8 / 335-4 337-8



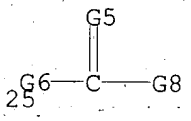


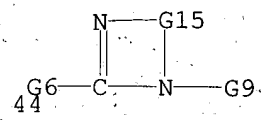


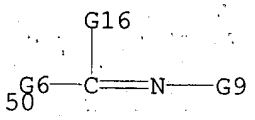


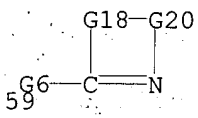
G3 = Hy<EC (8-9) A (1-) N (6-) C, AR (1-), BD (6-) N, RC (2), RS (0-1) E5 (1-2) E6 (0) OTHER> (SO)

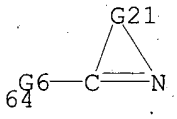
G4 = 25 / 44 / 50 / 59 / 64





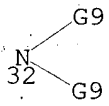




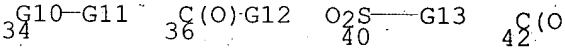


G5 = NH (SO) / O / S
G6 = NH / 29

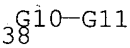
G7 = alkyl<(1-10)> / alkenyl<(2-6)> / alkynyl<(2-6)> / CH2Ph / CH2CH2Ph
G8 = 32 / Hy<EC (4-12) A (1-2) Q (1-2) N (0-1) O (0-1) S (0) OTHERQ, AN (1-) N, RC (1-2)> (SO (1-) G14)



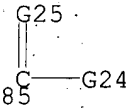
G9 = H / alkyl<(1-10)> (SO) / alkenyl<(2-6)> / alkynyl<(2-6)> / 34 / Cb<(3-8)> / Cb<EC (6-12) C, RC (2)> / aryl<RC (1-)> (SO) / heteroaryl<RC (1-)> (SO) / 36 / Hy<EC (4-12) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1)> (SO) / Hy<AR (0), BD (ALL) SE, RC (1-2)> / 40 / 42



G10 = alkylene<(1-10)>
G11 = aryl<RC (1-)> / heteroaryl<RC (1-)>
G12 = alkyl<(1-10)> / alkenyl<(2-6)> / alkynyl<(2-6)> / aryl<RC (1-)> / heteroaryl<RC (1-)> / 38 / Ph



G13 = alkyl<(1-10)> (SO) / aryl<RC (1-)> (SO) / heteroaryl<RC (1-)> (SO) / Hy<EC (4-12) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1)> (SO)
G14 = alkyl<(1-6)> / 85 / aryl<RC (1-)> / heteroaryl<RC (1-)> / OH



G15 = Ak<EC (1-9) C, BD (0-) D (0) T> (SO) /

R<TX "group to form optionally substituted ring">
G16 = H / alkyl<(1-10)> (SO G17) / Cb<(3-8)> /
Cb<EC (6-12) C, RC (2)> / aryl<RC (1-)> (SO) /
heteroaryl<RC (1-)> (SO) / Hy<EC (4-12) A (1-3) Q (0-) O (0-)
S (0-) N (0) OTHERQ, RC (1)> / alkenyl<(2-6)> /
alkynyl<(2-6)> / OH / SH / 55

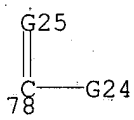
55 G18—G19

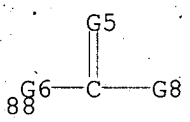
G17 = aryl<RC (1-)> (SO) / heteroaryl<RC (1-)> (SO)
G18 = O / S
G19 = alkyl<(1-10)> / 57 / aryl<RC (1-)> /
heteroaryl<RC (1-)> / alkenyl<(2-6)> / alkynyl<(2-6)>

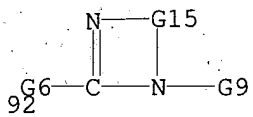
57 G10—G11

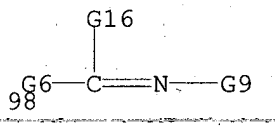
G20 = R<TX "group to form ring">
G21 = R<TX "group to form optionally substituted ring",
EC (1-) C>
G22 = alkyl<(1-10)> (SO (1-) G23) / OH /
alkoxy<(1-10)> (SO (1-) G23) / 73 / 77 / F / Cl / Br / I /
NO2 / NH2 / alkyl<(1-6)> (SR NH2) / alkylamino<(1-10)> /
dialkylamino<(1-10)> / CN / alkylthio<(1-10)> /
alkylsulfonyl<(1-10)> / **78** / alkenyl<(2-6)> (SR CO2H) /
alkenyl<(2-6)> (SR alkoxycarbonyl<(1-10)>) /
alkoxycarbonylamino<(1-10)> / NHCOMe / aryl<RC (1-)> /
heteroaryl<RC (1-)> / Cb<(3-8)> / SH /
Hy<EC (4-12) A (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ,
RC (1)> / Hy<EC (8-16) A (1-3) Q (0-) O (0-) S (0-) N (0)
OTHERQ (6-) C, AR (1-), BD (6-) N, RC (2), RS (1-) E6> / 88 /
92 / 98 / 103 / 108

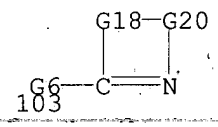
73 O—G11 77 O—G10—G11

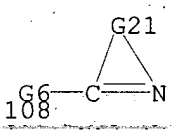












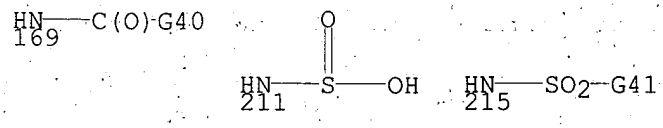
G23 = F / Cl / Br / I
G24 = **OH** / NH2 / SH / 80

80 G25—G26

G25 = **O** / S / NH
G26 = alkyl<(1-10)> / 82 / aryl<RC (1-)> /
heteroaryl<RC (1-)>

82 G10—G11

G27 = H / 169 / 211 / 215



G28 = NULL / alkylene (SO G29)
G29 = Cb<(3-8)> / aryl<RC (1-)> / heteroaryl<RC (1-)>
G30 = OH / SH / NH2 / 117

G31—G32
117

G31 = O / S / NH / 119

N—G32
119

G32 = alkyl<(1-10)> (SO (1-) G23) / alkenyl<(2-6)> / alkynyl<(2-6)> / alkoxy<(1-10)> (SR dialkylaminocarbonyl<(1-10)>) / aryl<RC (1-)> / heteroaryl<RC (1-)> / 121 / R<TX "sugar or steroid residue">

G10—G11
121

G34 = **(0-2) CH2**
G40 = OH / 207 / H / alkyl<(1-10)> / Cb<(3-8)> / 209 / aryl<RC (1-)> / heteroaryl<RC (1-)> / NH2 / 218 / pyrrolidino / piperidino / morpholino / Ph

O—G41 G10—G11 HN—G41
207 209 218

G41 = alkyl<(1-10)> / Cb<(3-8)> / 172 / aryl<RC (1-)> / heteroaryl<RC (1-)>

G10—G11
172

G43 = **Cb<EC (6) C, AR (1-), BD (6) N, RC (1), RS (1) E6> (SO (1-2) G22)** / phenylene
G44 = **Cb<EC (6) C, AR (1-), BD (6) N, RC (1), RS (1) E6> (SO (1-2) G22)** / m-C6H4
G45 = (0-3) CH2
G46 = H / alkyl<(1-10)> / aryl<RC (1-)> (SO) / heteroaryl<RC (1-)> (SO)
G54 = alkylene (SO) / NULL
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted

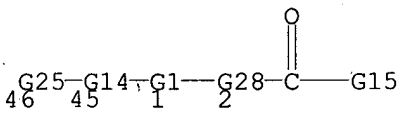
L3 ANSWER 33 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:346304 MARPAT

TITLE: Preparation of pyridinioarylcarbamoylindoline derivatives as serotonin receptor antagonists.
INVENTOR(S): Bromidge, Steven Mark
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK; Bromidge, Steven Mark
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

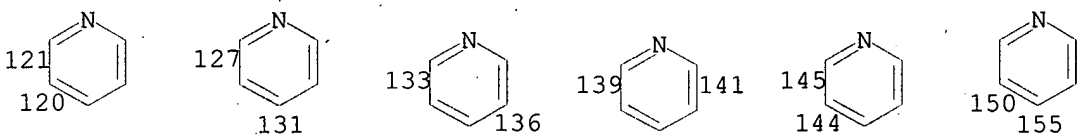
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9737989	A1	19971016	WO 1997-EP1611	19970326
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 891348	A1	19990120	EP 1997-915465	19970326
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2001508399	T2	20010626	JP 1997-535805	19970326
US 6028085	A	20000222	US 1998-155589	19980930
PRIORITY APPLN. INFO.:			GB 1996-7219	19960404
			WO 1997-EP1611	19970326

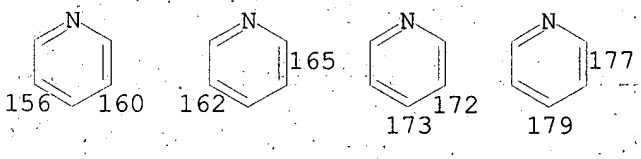
AB (R1)nP1A[P2(R2)m]NR3COR4 [R1, R2 = H, (substituted) alkyl; R3 = H, alkyl; R4 = (substituted) N-bonded bicycloheterocyclyl, aminopyrazinyl, aminopyridinyl, aminophenyl, etc.; P1, P2 = Ph, heterocyclyl contg. a quaternary N atom; A = bond, chain of 1-5 atoms (substituted) phenylene, heterocyclylene; n, m = 0-2], were prepd. as 5-HT2B/5-HT2C antagonists with increased soly./activity (no data). Thus, 5-methoxy-6-trifluoromethyl-1-[3-fluoro-5-(pyridin-3-yl)phenylcarbamoyl]indoline in MeCN was treated with sodium tetraphenylboron and bromomethyl acetate followed by 4 h reflux to give a tetraphenylborate salt which was subjected to ion exchange to give 100% 5-methoxy-6-trifluoromethyl-1-[3-fluoro-5-[1-(acetyloxy)methylpyridinium-3-yl]phenylcarbamoyl]indoline chloride.

MSTR 1A

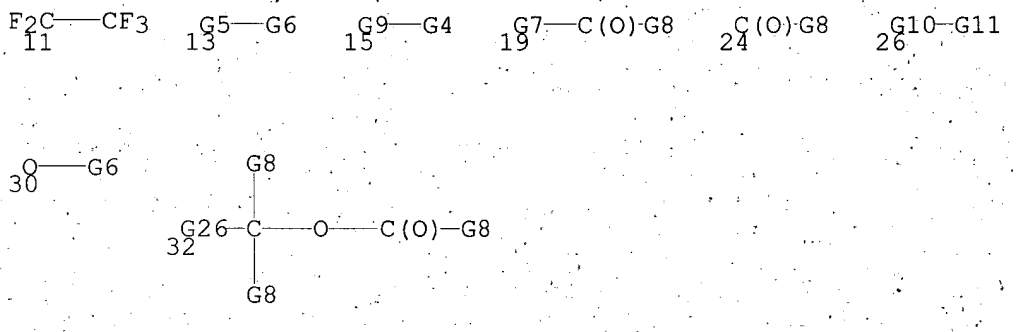


G1 = phenylene (SO (1-2) G2) /
Hy<EC (1-3) Q (1-) N (-2) O (-2) S (0) OTHERQ, CH (0-) +, RC (1-2)> (SO (1-2) G2) / (SC 121-45 120-2 / 127-45 131-2 / 133-45 136-2 / 139-45 141-2 / 144-45 145-2 / 150-45 155-2 / 156-45 160-2 / 162-45 165-2 / 173-45 172-2 / 179-45 177-2)





G2 = alkyl<(1-6)> (SO G3) / alkenyl<(2-6)> / alkynyl<(2-6)> / alkylthio<(1-6)> / CN / NO2 / X / CF3 / 11 / NH2 / 13 / 15 / 19 / CHO / OCF3 / SCF3 / 24 / 26 / OH / 30 / 32 / (SC F / Me)



G3 = NH2 / 7

G5—G6
7

G4 = NH2 / 17

G5—G6
17

G5 = NH / 9

N—G6
9

G6 = alkyl<(1-6)> / aryl (SO) / alkyl<(1-6)> (SR (1-) aryl (SO))

G7 = NH / 22

N—G6
22

G8 = H / alkyl<(1-6)> / aryl (SO) / alkyl<(1-6)> (SR (1-) aryl (SO))

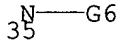
G9 = C(O) / S(O) / SO2

G10 = CH2 / **C(O)**

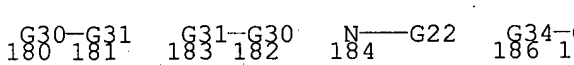
G11 = **OH** / 28

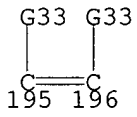
O—G6
28

G12 = NH / 35

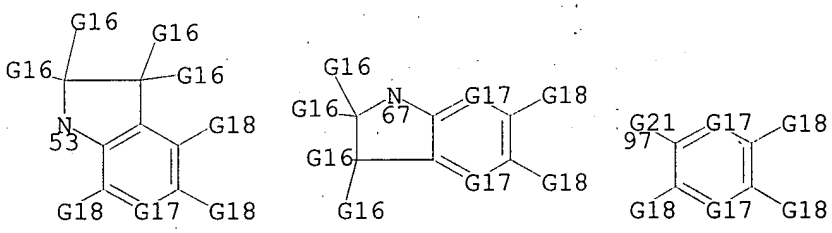


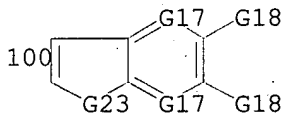
G13 = R<TX "counter ion"> / (EX halogen anion / chloride / bromide)
G14 = R<TX "chain of 1 to 5 atoms"> / phenylene (SO) / Hy<EC (1-3) Q (0-) O (0-) S (0-) N (0) OTHERQ, RS (0-) E5 (0-) E6 (0-) E7 (0) OTHER> (SO) / (EX 180-46 181-1 / 183-46 182-1 / NH / 184 / 186-46 187-1 / 189-46 188-1 / 192-46 194-1 / C(O) / CHOH / alkylene / 195-46 196-1 / O / S(O) / SO2)





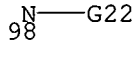
G15 = 53 / 67 / 97 / 100



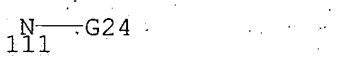


G16 = H / alkyl<(1-6)>
G17 = N / 60

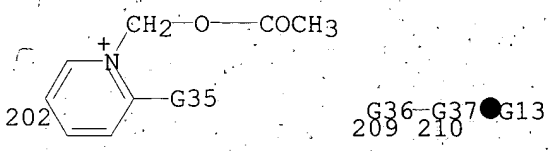
G18 = H / R / (SC CF3 / OMe)
G21 = NH / 98



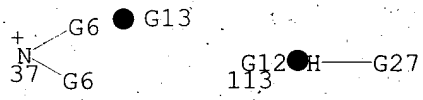
G22 = alkyl<(1-6)>
G23 = O / S / CH2 / 111



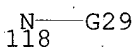
G24 = H / alkyl<(1-6)>
G25 = **Ph (SO (1-2) G2)** / Hy<EC (1-3) Q (1-) N (-2) O (-2) S (0) OTHERQ, CH (0-) +, RC (1-2)> (SO (1-2) G2) / (SC 209 / pyridyl / 202)



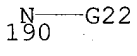
G26 = 113 / 37



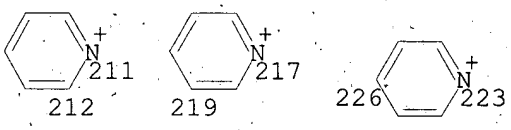
G27 = R<TX."counter ion"> / (EX X / Cl / Br)
G28 = NH / 118



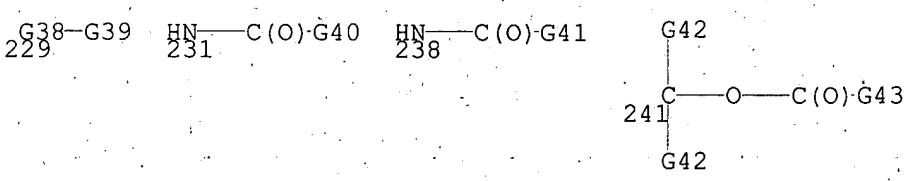
G29 = alkyl<(1-6)>
G30 = **(1-4) CH2**
G31 = C(O) / **O** / S / S(O) / SO2
G32 = NH / 190

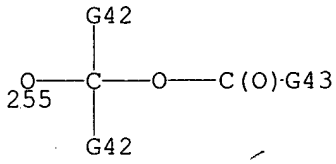


G33 = H / F
G34 = C(O) / SO2
G35 = H / Me
G36 = 219-45 217-210 / 226-45 223-210 / 212-45 211-210

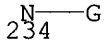


G37 = alkyl<(1-6)> / alkoxy<(1-6)> / O / NH2 / 229 / 231 / 238 / 241 / 255

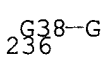




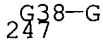
G38 = NH / 234



G39 = alkyl<(1-20)> / aryl (SO) /
alkyl<(1-6)> (SR (1-) aryl (SO))
G40 = NH2 / 236



G41 = H / alkyl<(1-20)> / aryl (SO) /
alkyl<(1-6)> (SR (1-) aryl (SO))
G42 = H / R
G43 = H / alkyl<(1-20)> / aryl (SO) /
alkyl<(1-6)> (SR (1-) aryl (SO)) / NH2 / 247



MPL: claim 1
NTE: oxygen alternative in G37 is free radical

L3 ANSWER 34 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:220648 MARPAT
TITLE: Preparation of cyclic amic acid derivatives as protein-farnesyl transferase (PFT) inhibitors
INVENTOR(S): Aoyama, Tetsuya; Kawakami, Kumiko; Arai, Sachie; Satoh, Toshihiko; Monden, Yoshiaki
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan; Aoyama, Tetsuya; Kawakami, Kumiko; Arai, Sachie; Satoh, Toshihiko; Monden, Yoshiaki
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729078	A1	19970814	WO 1997-JP303	19970207

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2244695	AA	19970814	CA 1997-2244695	19970207
AU 9716191	A1	19970828	AU 1997-16191	19970207
EP 882703	A1	19981209	EP 1997-902605	19970207
EP 882703	B1	20020814		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 222234	E	20020815	AT 1997-902605	19970207
US 6011174	A	20000104	US 1998-117534	19980804
PRIORITY APPLN. INFO.:			JP 1996-45500	19960207
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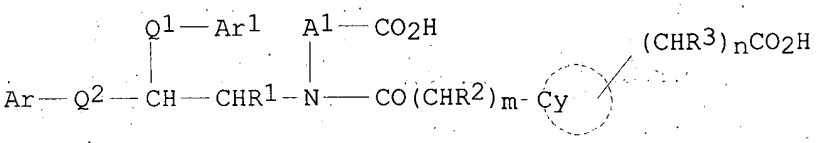
			WO 1997-JP303	19970207

GI



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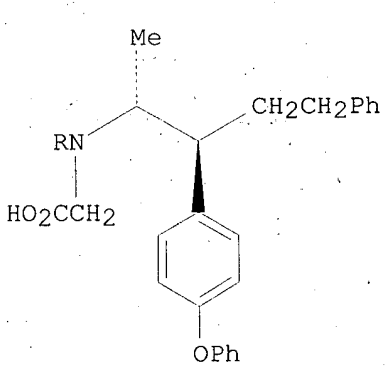
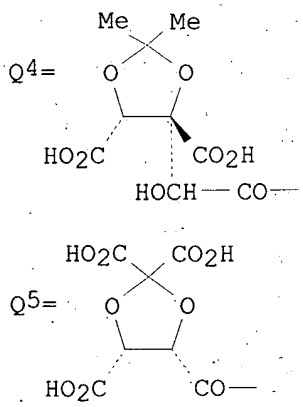


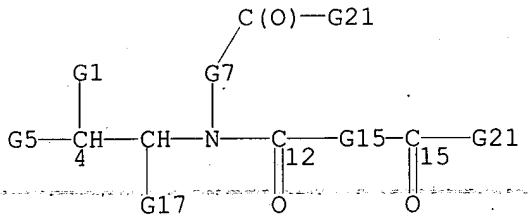
II



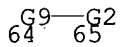
AB Compds. represented by general formula [I; Ar1 = aryl or heteroaryl; Ar = Ar3-Q3-Ar2-, Ar2; wherein Ar2, Ar3 = aryl, heteroaryl; Q3 = a single bond, oxygen, sulfur, methylene, vinylene, or a group represented by CO, NH, CO2, O2C, CH2CH2, OCH2, SCH2, CH2O, CH2S, NHCO, or CONH; Cy = aryl, heteroaryl, or an alicyclic group optionally having one or two oxygen atoms; A1 = C1-4 hydrocarbyl; Q1 = a single bond, a group represented by CH2O, OCH2, CH2S, or SCH2, or C1-6 hydrocarbyl; Q2 = a single bond or a group represented by (CH2)l or -(CH2)q-W-(CH2)p; R1 = lower alkyl; wherein l = an integer of 1 to 6; p, q = an integer of 0 to 3; R2, R3 = H, OH, or lower alkyl; W = oxygen, sulfur, vinylene, or ethynylene; m = an integer of 0 to 2; n = 0 or 1] or pharmacol. acceptable salts or esters thereof, which inhibits functional expression of cancer gene Ras protein by inhibiting PFT in vivo and exhibit antitumor activity, are prepd. An antitumor agent comprising these compds. as the active ingredients is claimed. These compds. also inhibit transfection of ras and thereby reactivation of HIV gene incorporated into host cells and are also useful as anti-HIV agents. Thus, N-(methoxycarbonylmethyl)-[(1R,2R)-1-methyl-2-(4-phenoxyphenyl)-4-phenylbutyl]amine (prepn. given) was condensed with di-Me 2-(1-acetoxycarboxymethyl)-2,3-O-isopropylidene-L-tartrate (prepn. given) using 2-chloro-1,3-dimethylimidazolium chloride in the presence of Et3N in CHCl3 at room temp. for 4 h followed by sapon. with a mixt. of 1 N aq. NaOH and THF to give the title compd. (II.3Na; R = Q4). II.3Na (R = Q4) and II (R = Q5) showed IC50 of 0.16 and 0.075 nM, resp., against PFT

and IC50 of 0.24 and 2.0 .mu.M, resp., against farnesylation of Ras protein in NIH3T3 cells expressing activated ras gene.

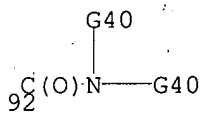
MSTR 1



G1 = Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G2) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G2) / Ph / naphthyl / anthracenyl / 64

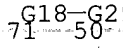


G2 = F / Cl / Br / I / OH / NH2 / NO2 / CN / CO2H / alkoxycarbonyl<(1-6)> / 92 / alkyl<(1-6)> (SO OH) / alkenyl<(2-6)> / alkoxy<(1-6)> / alkyl<(1-6)> (SR (1-) F) / Ph / naphthyl / anthracenyl / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ>

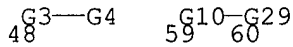


G3 = **Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G31)** / heteroarylene<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G31)

G4 = Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G31) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G31) / Ph / naphthyl / anthracenyl / 71



G5 = 48 / 59



G6 = F / Cl / Br / I / alkyl<(1-6)>

G7 = Ak<EC (1-4) C, BD (0) T, DC (0) M3> (SO (1-) G8)

G8 = F / Cl / Br / I / OH / alkyl<(1-6)> (SO OH) / alkoxy<(1-6)>

G9 = 66-4 67-65 / 69-4 68-65 / Ak<EC (1-6) C, BD (0) T, DC (0) M3> (SO (1-) G6)

H_2C——G27 G27—CH_2
66 67 69 68

G10 = alkylene<EC (1-6) C, DC (0) M3> / O / S / CH=CH / ethynylene / 16-4 18-60 / 20-4 21-60 / 22-4 23-60

G11—G12—G11 G13—G11 G11—G14
16 18 20 21 22 23

G11 = alkylene<EC (1-3) C, DC (0) M3>
G12 = O / S / CH=CH / ethynylene
G13 = O / S / CH=CH / ethynylene
G14 = O / S / CH=CH / ethynylene
G15 = Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G32) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G32) / Cb<AR (0)> (SO (1-) G32) / Hy<EC (1-2) O, AR (0)> (SO (1-) G32) / 78 / 80-12 81-15 / 82-12 83-15 / 84-12 86-15

G35=O G36—G37 G37—G38 G36—G37—G38
78 80 81 82 83 84 86

G17 = alkyl<(1-6)>
G18 = O / S / CH2 / CH=CH / C(O) / NH / 51-48 52-50 / 53-48 54-50 / CH2CH2 / **55-48 56-50** / 57-48 58-50

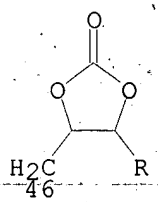
C(O)G28 G28—C(O) G27—CH_2 H_2C——G27
51 52 53 54 55 56 57 58

G19 = Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER>
G20 = Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G2) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G2) / Ph / naphthyl / anthracenyl
G21 = OH / 25

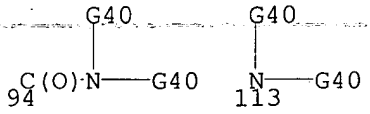
O——G22
25

G22 = R / (EX alkyl<(1-6)> / cycloalkyl<(3-6)> / alkyl (SR (1-) G19) / alkenyl<(2-6)> / alkyl<(1-6)> (SR alkoxy<(1-6)>) / alkyl<(1-6)> (SR G26) / alkyl<(1-6)> (SR alkoxycarbonyl<(1-6)>) / alkyl<(1-6)> (SR CO2H) / alkyl<(1-6)> (SR alkoxycarbonyloxy<(1-6)>) / alkyl<(1-6)> (SR OCONH2 (SO)) / 37 / 46)

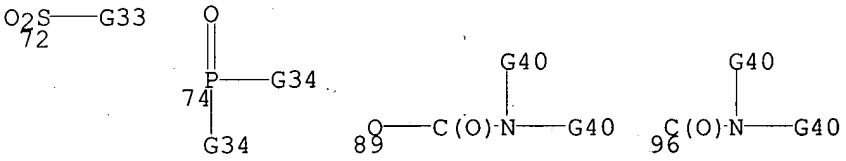
C(O)—o-C_6H_4—CO_2H
37



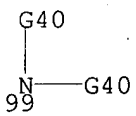
G26 = OCHO / alkylcarbonyloxy<(1-5)>
G27 = **O** / S
G28 = O / NH
G29 = **Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G31)** / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G31) / Ph / naphthyl / anthracenyl
G31 = F / Cl / Br / I / OH / 113 / NO2 / CN / **CO2H** / alkoxycarbonyl<(1-6)> / 94 / alkyl<(1-6)> (SO OH) / alkenyl<(2-6)> / alkoxy<(1-6)> (SO (1-) G19) / alkyl<(1-6)> (SR (1-) F)



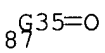
G32 = F / Cl / Br / I / OH / NH2 / NO2 / CN / CO2H / 96 / alkyl<(1-6)> (SO 89) / alkenyl<(2-6)> / alkyl<(1-6)> (SR OH) / alkyl<(1-6)> (SR (1-) F) / alkoxy<(1-6)> / alkyl<(1-6)> (SR alkoxy<(1-6)>) / SO3H / 72 / Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ> / 74



G33 = alkoxy<(1-6)> / 99



G34 = OH / alkoxy<(1-6)>
G35 = Cb<AR (0)> (SO (1-) G32) / Hy<EC (1-2) O, AR (0)> (SO (1-) G32)
G36 = alkylene<(1-14)> (SO OH)
G37 = Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G32) / heteroaryl<EC (1-2) Q (0-) N (0-) O (0-) S (0) OTHERQ> (SO (1-) G32) / Cb<AR (0)> (SO (1-) G32) / Hy<EC (1-2) O, AR (0)> (SO (1-) G32) / 87



G38 = alkylene<(1-7)> (SO OH)
G40 = H / alkyl<(1-6)>
DER: or pharmaceutically acceptable salts
MPL: claim 1

L3 ANSWER 35 OF 55 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 127:176338 MARPAT
TITLE: Preparation of substituted amide derivatives as protein-farnesyl transferase inhibitors
INVENTOR(S): Iwasawa, Yoshikazu; Aoyama, Tetsuya; Kawakami, Kumiko; Arai, Sachie; Satoh, Toshihiko; Monden, Yoshiaki
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan; Iwasawa, Yoshikazu; Aoyama, Tetsuya; Kawakami, Kumiko; Arai, Sachie; Satoh, Toshihiko; Monden, Yoshiaki
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729073	A1	19970814	WO 1997-JP304	19970207
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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AU 9716192	A1	19970828	AU 1997-16192	19970207
EP 882701	A1	19981209	EP 1997-902606	19970207
EP 882701	B1	20020724		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 221045	E	20020815	AT 1997-902606	19970207
US 6048894	A	20000411	US 1998-117533	19980804
PRIORITY APPLN. INFO.:			JP 1996-45502	19960207
			WO 1997-JP304	19970207

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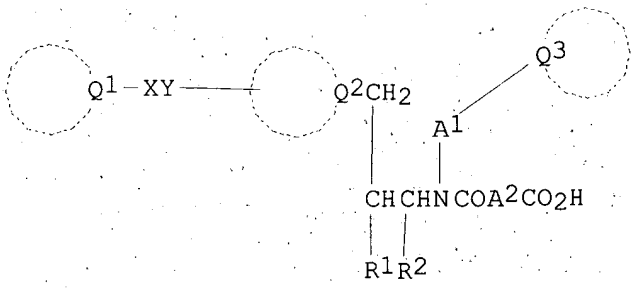
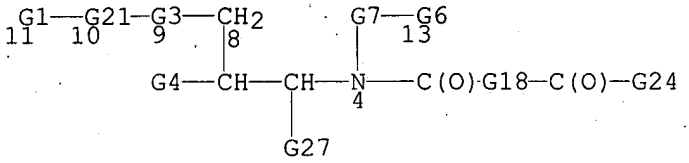


I

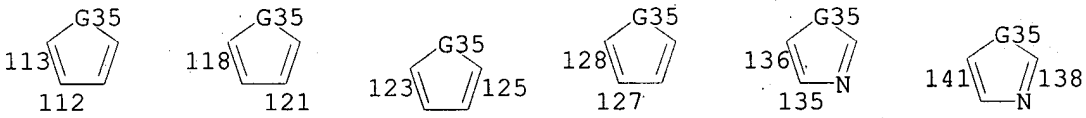
AB The title compds. I [Q1, Q2, Q3 each represents aryl or heteroaryl; A1 represents hydrocarbyl, etc.; A2 represents hydrocarbyl; R1 represents lower alkyl, lower alkenyl, lower alkoxy, carboxy, lower alkoxycarbonyl, carbamoyl, lower alkylcarbamoyl, etc.; R2 represents lower alkyl; and X and Y each represents oxygen, sulfur, carbonyl, etc.; or X and Y are bonded to each other to thereby form vinylene or ethynylene; a proviso is given] are prepd. In an in vitro test for protein farnesyl transferase inhibiting activity, 3-(ethoxycarbonyl)-4-hydroxy-4-[N-[(1RS,2RS)-2-(isopropoxycarbonyl)-1-methyl-3-[5-(phenylcarbamoyl)-2-furyl]propyl]-N-(2-naphthylmethyl)carbamoyl]-3-butenoic acid showed IC50 of 3.1 nM.

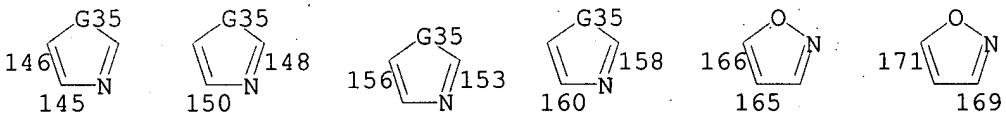
MSTR 1

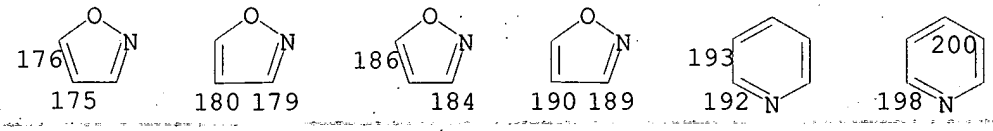


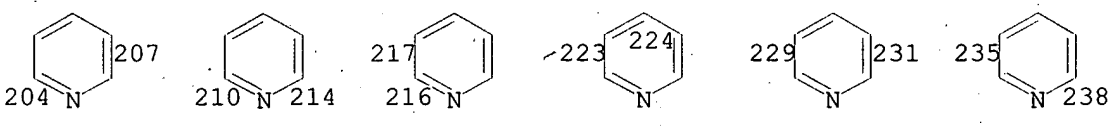
G1 = **Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G5)** / Ph / naphthyl / anthracenyl / heteroaryl<EC (1-2) Q (0-) O (0-) N (0-) S (0) OTHERQ> (SO (1-) G5) / (SC thienyl)

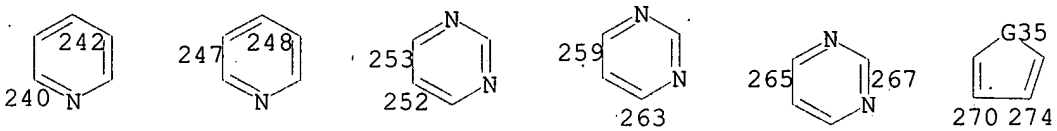
G3 = **Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G5)** / heteroarylene<EC (1-2) Q (0-) O (0-) N (0-) S (0) OTHERQ> (SO (1-) G5) / (EX phenylene / 113-10 112-8 / 118-10 121-8 / 123-10 125-8 / 127-10 128-8 / 270-10 274-8 / 136-10 135-8 / 141-10 138-8 / 145-10 146-8 / 150-10 148-8 / 153-10 156-8 / 158-10 160-8 / 166-10 165-8 / 171-10 169-8 / 175-10 176-8 / 180-10 179-8 / 184-10 186-8 / 189-10 190-8 / 192-10 193-8 / 198-10 200-8 / 204-10 207-8 / 210-10 214-8 / 217-10 216-8 / 223-10 224-8 / 229-10 231-8 / 235-10 238-8 / 242-10 240-8 / 248-10 247-8 / 253-10 252-8 / 259-10 263-8 / 265-10 267-8 / 275-10 276-8 / 281-10 286-8 / 287-10 290-8 / 296-10 294-8 / 302-10 299-8 / 308-10 310-8)

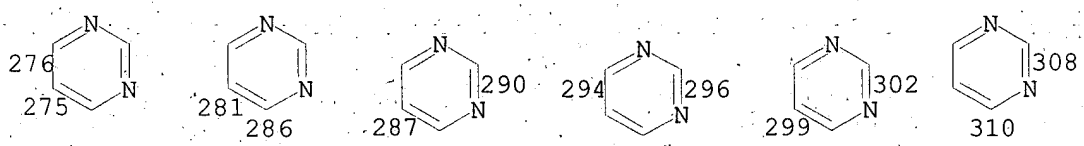




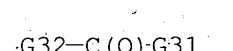








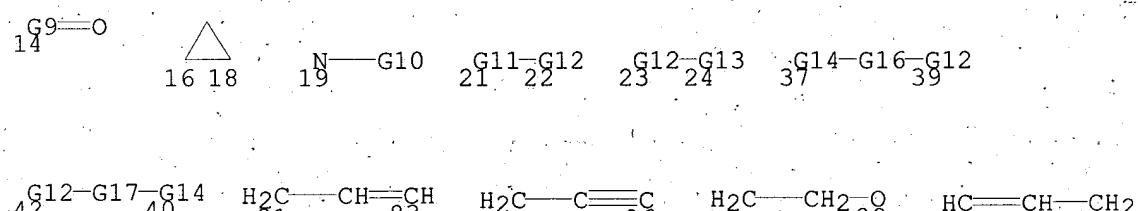
G4 = alkyl<(1-6)> (SO G30) / alkenyl<(2-6)> (SO G30) / alkoxy<(1-6)> / CO2H / alkoxycarbonyl<(1-6)> / CONH2 / alkylaminocarbonyl<(1-6)> / dialkylaminocarbonyl<(1-6)> / 107 / Cb<AR (0)> (SO (1-) G34) / Hy<EC (1-2) O (-2) N (0) OTHERQ, AR (0)> (SO (1-) G34)



G5 = F / Cl / Br / I / OH / NH2 / NO2 / CN / **CO2H (SO)** / alkoxycarbonyl<(1-6)> / CONH2 / alkylaminocarbonyl<(1-6)> / dialkylaminocarbonyl<(1-6)> / alkyl<(1-6)> (SO OH) / alkyl<(1-6)> (SR (1-) F) / alkoxy<(1-6)> / alkenyl<(2-6)>

G6 = Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (-2) G5) / Ph / naphthyl / anthracenyl / heteroaryl<EC (1-2) Q (0-) O (0-) N (0-) S (0) OTHERQ> (SO (-2) G5) / (SC thienyl / benzothienyl / benzofuranyl)

G7 = Ak<EC (1-6) C, BD (0) T, DC (0) M3> (SO (1-) G8) / 14 / O / S / ethynylene / 16-4 18-13 / 19 / 21-4 22-13 / 23-4 24-13 / 37-4 39-13 / 42-4 40-13 / (SC 81-4 83-13 / 84-4 86-13 / 87-4 89-13 / 92-4 90-13 / 95-4 93-13 / 98-4 96-13 / CH2CH2CH2)

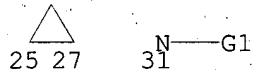


G8 = F / Cl / Br / I / alkyl<(1-6)> (SO OH) / alkoxy<(1-6)>

G9 = Ak<EC (1-6) C, BD (0) T, DC (0) M3> (SO (1-) G8)

G10 = H / alkyl<(1-6)>

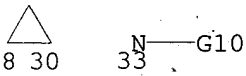
G11 = O / S / ethynylene / 25-4 27-22 / 31



G12 = Ak<EC (1-5) C, BD (0) T, DC (0) M3> (SO (1-) G8) / 35

G28=O
35

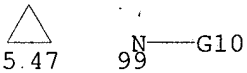
G13 = O / S / ethynylene / 28-23 30-13 / 33



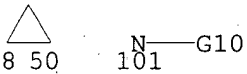
G14 = Ak<EC (1-4) C, BD (0) T, DC (0) M3> (SO (1-) G8) /
43

G15=O
43

G15 = Ak<EC (1-4) C, BD (0) T, DC (0) M3> (SO (1-) G8)
G16 = O / S / ethynylene / 45-37 47-39 / 99



G17 = O / S / ethynylene / 48-42 50-40 / 101



G18 = Ak<EC (1-8) C, BD (0) T, DC (0) M3> (SO (1-) G19)
G19 = F / Cl / Br / I / alkyl<(1-6)> (SO OH) / OH /
alkoxy<(1-6)> / CO2H (SO) / alkoxycarbonyl<(1-6)> /
alkenyloxycarbonyl<(2-6)> / alkyl<(1-6)> (SR CO2H (SO)) /
Ph / naphthyl / anthracenyl / alkyl<(1-6)> (SR (1-) G20)
G20 = Ph / naphthyl / anthracenyl
G21 = 51-11 52-9 / 53-11 54-9 / 59-11 60-9 / CH=CH /
ethynylene

G22—G23 G23—G22 G23—G23
51 52 53 54 59 60

G22 = O / S / 55

N——G10
55

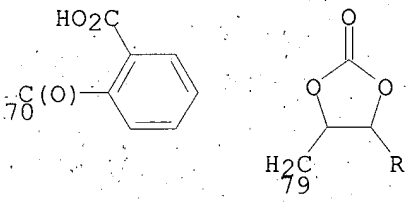
G23 = C(O) / **57**

HC——G10
57

G24 = OH / 62

O—G25
62

G25 = R / (EX alkyl<(1-6)> / cycloalkyl<(3-6)> / alkyl<(1-6)> (SR (1-) G19) / alkenyl<(2-6)> / alkyl<(1-6)> (SR alkoxy<(1-6)>) / alkyl<(1-6)> (SR G26) / alkyl<(1-6)> (SR alkoxycarbonyl<(1-6)>) / alkyl<(1-6)> (SR CO2H) / alkyl<(1-6)> (SR alkoxycarbonyloxy<(1-6)>) / alkyl<(1-6)> (SR OCONH2 (SO)) / 70 / 79)



G26 = OCHO / alkylcarbonyloxy<(1-5)>
G27 = alkyl<(1-6)>
G28 = Ak<EC (1-5) C, BD (0) T, DC (0) M3> (SO (1-) G8)
G29 = alkylamino<(1-6)> / dialkylamino<(1-6)>
G30 = OH / alkoxy<(1-6)> / alkoxycarbonyl<(1-6)> / CONH2 / alkylaminocarbonyl<(1-6)> / dialkylaminocarbonyl<(1-6)> / 103

C(O)NH—G29
103

G31 = H / NH2 / alkyl<(1-6)> / alkoxy<(1-6)> / alkylamino<(1-6)> / dialkylamino<(1-6)>
G32 = O / 110

N—G33
110

G33 = H / alkyl<(1-6)>
G34 = F / Cl / Br / I / OH / NH2 / NO2 / CN / CO2H / alkyl<(1-6)> (SO (1-) OH) / alkenyl<(2-6)> / alkoxy<(1-6)> / alkyl<(1-6)> (SR (1-) F) / alkoxycarbonyl<(1-6)> / CONH2 / alkylaminocarbonyl<(1-6)> / dialkylaminocarbonyl<(1-6)>
G35 = O / S
DER: or pharmaceutically acceptable salts
MPL: claim 1

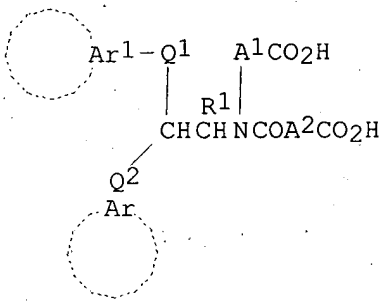
L3 ANSWER 36 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:176275 MARPAT
TITLE: Preparation of substituted amide derivatives as antitumor agents
INVENTOR(S): Iwasawa, Yoshikazu; Aoyama, Tetsuya; Kawakami, Kumiko; Arai, Sachie; Satoh, Toshihiko; Monden, Yoshiaki
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan; Iwasawa, Yoshikazu; Aoyama, Tetsuya; Kawakami, Kumiko; Arai, Sachie; Satoh, Toshihiko; Monden, Yoshiaki
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

Searched by Barb O'Bryen, STIC 308-4291

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729077	A1	19970814	WO 1997-JP302	19970207
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9716190	A1	19970828	AU 1997-16190	19970207
PRIORITY APPLN. INFO.:			JP 1996-45501	19960207
			WO 1997-JP302	19970207

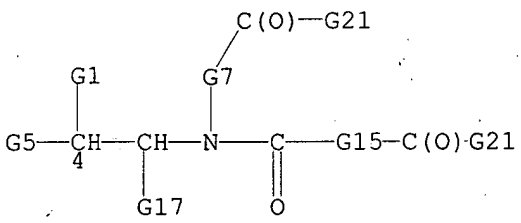
GI



I

AB The title compds. I [Ar1 represents aryl or heterocyclic arom. group; Ar represents aryl, etc.; A1 represents C1 - C4 hydrocarbyl; A2 represents C1 - C8 hydrocarbyl; m is an integer of 1 to 6; Q1 represents a single bond, a group represented by CH2O, etc.; Q2 represents a single bond or a group represented by -(CH2)m, etc.; R1 represents lower alkyl] are prepd. (2R)-2-[N-(carboxymethyl)-N-[(1R,2R)-1-methyl-2-(4-phenoxyphenyl)-4-phenylbutyl]carbamoylmethyl]succinic acid in vitro showed IC50 of 0.2 nM (against protein farnesyl transferase) and IC50 of 2.9 .mu.M (against ras protein farnesylation).

MSTR 1



G1 = Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G2) / heteroaryl (SO (1-) G2) / Ph (SO) / naphthyl (SO) / anthracenyl (SO) / 64 / (SC thienyl)

G9—G29
64 65

G2 = F / Cl / Br / I / OH / NH2 / NO2 / CN / **CO2H** /
alkoxycarbonyl<(1-6)> / CONH2 / alkylaminocarbonyl<(1-6)> /
dialkylaminocarbonyl<(1-6)> / alkyl<(1-6)> (SO OH) /
alkenyl<(2-6)> / alkoxy<(1-6)> / alkyl<(1-6)> (SR (1-) F) /
Ph / naphthyl / anthracenyl / heteroaryl
G3 = **Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3),**
RS (1-3) E6 (0) OTHER> (SO (1-) G31) /
heteroarylene (SO (1-) G31)
G4 = Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3),
RS (1-3) E6 (0) OTHER> (SO (1-) G31) /
heteroaryl (SO (1-) G31) / Ph (SO) / naphthyl (SO) /
anthracenyl (SO) / 71

G18—G29
71 50

G5 = 48 / 59

G3—G4 G10—G29
48 59 60

G6 = F / Cl / Br / I / alkyl<(1-6)>
G7 = Ak<EC (1-4) C, DC (0) M3> (SO (1-) G8)
G8 = F / Cl / Br / I / OH / alkyl<(1-6)> (SO OH) /
alkoxy<(1-6)>
G9 = 66-4 67-65 / 69-4 68-65 /
Ak<EC (1-6) C, DC (0) M3> (SO (1-) G6)

H2C—G27 G27—CH2
66 67 69 68

G10 = alkylene<EC (1-6) C, DC (0) M3> / O / S / CH=CH /
ethynylene / 16-4 18-60 / 20-4 21-60 / 22-4 23-60

G11—G12—G11 G13—G11 G11—G14
16 18 20 21 22 23

G11 = alkylene<EC (1-3) C, DC (0) M3>
G12 = O / S / CH=CH / ethynylene
G13 = O / S / CH=CH / ethynylene
G14 = O / S / CH=CH / ethynylene
G15 = Ak<EC (1-8) C, DC (0) M3> (SO (1-) G16)
G16 = F / Cl / Br / I / alkyl<(1-6)> (SO OH) / OH /
alkoxy<(1-6)> / CO2H / alkyl<(1-6)> (SR CO2H) /
alkyl<(1-6)> (SR (1-) G19) / Ph / naphthyl / anthracenyl
G17 = alkyl<(1-6)>
G18 = O / S / CH2 / CH=CH / C(O) / NH / 51-48 52-50 /
53-48 54-50 / CH2CH2 / **55-48 56-50** / 57-48 58-50

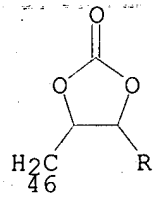
C(O)G28 G28—C(O) G27—CH2 H2C—G27
51 52 53 54 55 56 57 58

G19 = Ph / naphthyl / anthracenyl
G21 = OH / 25

25 O—G22

G22 = R / (EX alkyl<(1-6)> / cycloalkyl<(3-6)> / alkyl (SR (1-) G19) / alkenyl<(2-6)> / alkyl<(1-6)> (SR alkoxy<(1-6)>) / alkyl<(1-6)> (SR G26) / alkyl<(1-6)> (SR alkoxycarbonyl<(1-6)>) / alkyl<(1-6)> (SR CO2H) / alkyl<(1-6)> (SR alkoxycarbonyloxy<(1-6)>) / alkyl<(1-6)> (SR OCONH2 (SO)) / 37 / 46)

37 C(O)—o-C6H4—CO2H



G26 = OCHO / alkylcarbonyloxy<(1-5)>
G27 = O / S
G28 = O / NH
G29 = **Cb<EC (6-14) C, AR (1-), BD (ALL) N, RC (1-3), RS (1-3) E6 (0) OTHER> (SO (1-) G2)** / heteroaryl (SO (1-) G2) / Ph (SO) / naphthyl (SO) / anthracenyl (SO) / (SC thienyl)
G31 = F / Cl / Br / I / OH / NH2 / NO2 / CN / **CO2H** / alkoxycarbonyl<(1-6)> / CONH2 / alkylaminocarbonyl<(1-6)> / dialkylaminocarbonyl<(1-6)> / alkyl<(1-6)> (SO OH) / alkenyl<(2-6)> / alkoxy<(1-6)> / alkyl<(1-6)> (SR (1-) F)
DER: or pharmaceutically acceptable salts
MPL: claim 1

L3 ANSWER 37 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:344209 MARPAT
TITLE: Liquid crystalline acrylates or .alpha.-substituted acrylates, curable dental compositions containing these compounds, and methods for using these compositions
INVENTOR(S): Klee, Joachem E.; Frey, Holger; Holter, Dirk; Mulhaupt, Rolf
PATENT ASSIGNEE(S): Dentsply International, Inc., USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9714674	A1	19970424	WO 1996-US16436	19961016
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5998499	A	19991207	US 1996-723443	19961007
EP 861230	A1	19980902	EP 1996-936465	19961016
EP 861230	B1	20020102		
R: CH, DE, FR, GB, LI				
JP 2001509128	T2	20010710	JP 1997-515908	19961016

PRIORITY APPLN. INFO.: US 1995-543950 19951017
US 1996-723443 19961007
US 1994-217998 19940325
US 1994-231535 19940422
WO 1996-US16436 19961016

AB CH2:CR4CO2[CH2CH(OXR3M)CH2OR1O]nCH2CH(OXR3M)CH2OCOCR4:CH2 [I; R1 = A, AY1B, AY1BY2C, or a steroidal group; A, B, C = (substituted) C6-24 arom. group, (substituted) C2-24 heteroarom. group, (substituted) C5-30 cycloalkylene, (substituted) C2-20 alkylene; Y1, Y2 = covalent bond, OCO, N:N, CH:N, C:C, CO, O(CO)O, O, S, SO2, OCS, CH2O, CH2S, C.tplbond.C, CL1:CL2, CL1:CL2CO2, CL1:CL2CO, N(O):N; L1, L2 = H, C1-20 alkyl, or CN; R3 = H, (substituted) C1-20 alkylene, C1-20 oxyalkylene, C1-20 thioalkylene, or C1-20 carboxyalkylene; R4 = H, (substituted) C1-20 alkyl, C5-12 cycloalkyl, C6-20 aryl, M = mesogenic AZ, AY1BZ, AY1BY2CZ, or a steroidal group; Z = H, halo, CN, OR, CO2R, NO2, (halo-substituted) C1-20 alkylene or alkenylene, (halo-substituted) C1-20 oxyalkylene or oxyalkylenylene, (halo-substituted) C1-20 thioalkylene or thioalkenylene, (halo-substituted) C1-20 carboxyalkylene or carboxyalkylenylene; X = covalent bond, CO, NHCO, or OCO; n = 1-10]. I polymerize quant. and with vol. shrinkage <2.5% using redox and(or) photochem. initiators and are useful in dental compns. A typical monomer was manufd. by esterification of 4,4'-bis(2-hydroxy-3-methacryloyloxypropoxy)biphenyl with 4'-cyanobiphenyl-4-oxyvaleric acid.

MSTR 2

G21—G10—G15—G20
104 105 109 123

G4 = O / S
G5 = alkenylene (SO CN)
G6 = CH / 46

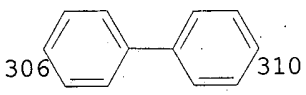
N═O
46

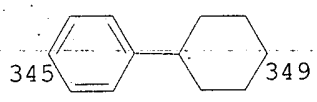
G10 = NULL / alkylene<(1-20)> (SO) / 356-104 357-109 / 358-104 360-109

G11—G12 G11—C(O)—O
356 357 358 360

G11 = alkylene<(1-20)>
G12 = O / S
G15 = arylene<(6-24)> (SO) / heteroarylene<(2-24)> (SO) / cycloalkylene<(5-30)> (SO) / 125-105 127-123 / 152-105 156-123 / R<TX "steroid moiety"> / (EX 306-105 310-123 / 345-105 349-123)

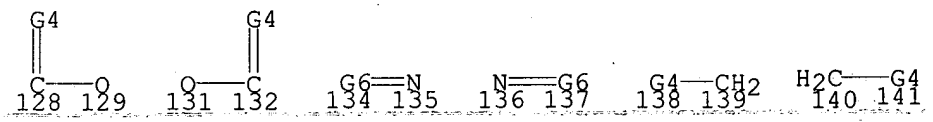
G16—G17—G16 G16—G18—G16—G19—G16
125 127 152 154 156

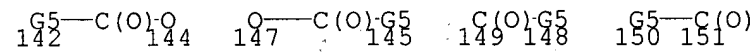




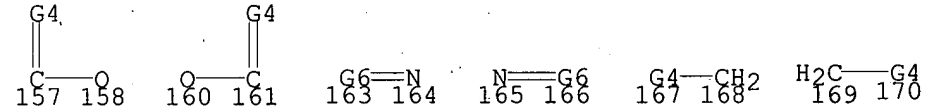
G16 = **arylene<(6-24)> (SO)** / heteroarylene<(2-24)> (SO) / cycloalkylene<(5-30)> (SO)

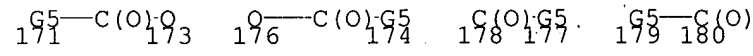
G17 = NULL / 128-125 129-127 / 131-125 132-127 / N=N / 134-125 135-127 / 136-125 137-127 / OCO2 / O / S / SO2 / **138-125 139-127** / 140-125 141-127 / ethynylene / CH=CH / alkenylene (SO CN) / 142-125 144-127 / 147-125 145-127 / 149-125 148-127 / 150-125 151-127



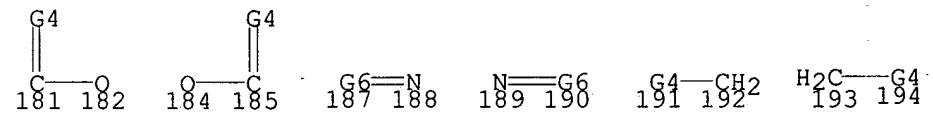


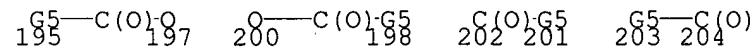
G18 = NULL / 157-152 158-154 / 160-152 161-154 / N=N / 163-152 164-154 / 165-152 166-154 / OCO2 / O / S / SO2 / 167-152 168-154 / 169-152 170-154 / ethynylene / CH=CH / alkenylene (SO CN) / 171-152 173-154 / 176-152 174-154 / 178-152 177-154 / 179-152 180-154





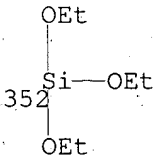
G19 = NULL / 181-154 182-156 / 184-154 185-156 / N=N / 187-154 188-156 / 189-154 190-156 / OCO2 / O / S / SO2 / 191-154 192-156 / 193-154 194-156 / ethynylene / CH=CH / alkenylene (SO CN) / 195-154 197-156 / 200-154 198-156 / 202-154 201-156 / 203-154 204-156





G20 = H / X / CN / OH (SO) / **CO2H (SO)** / NO2 / alkyl<(1-20)> (SO (1-) X) / alkenyl<(2-20)> (SO (1-) X) / alkoxy<(1-20)> (SO (1-) X) / alkenyloxy<(2-20)> (SO (1-) X) / alkylthio<(1-20)> (SO (1-) X) / alkenylthio<(2-20)> (SO (1-) X) / alkylcarbonyloxy<(1-20)> (SO) / alkenylcarbonyloxy<(2-20)> (SO (1-) X)

G21 = H / OMe / OH / Cl / Br / **CO2H** / NCO / 352 / R

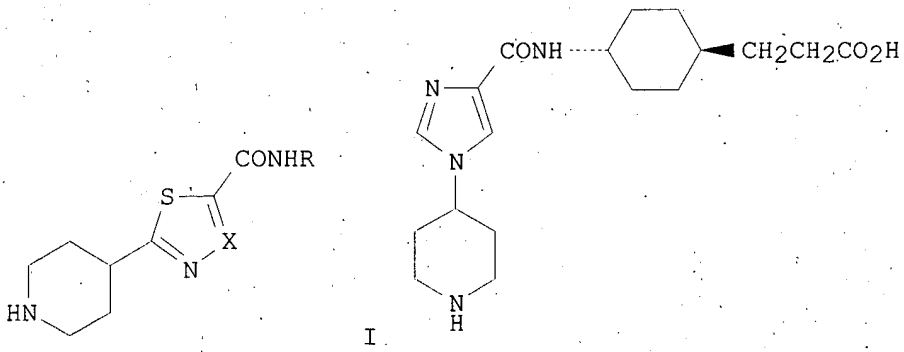


MPL: claim 8
NTE: also incorporates claim 14

L3 ANSWER 38 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:343567 MARPAT
TITLE: Five-membered heterocycles for use as antithrombics and platelet aggregation inhibitors
INVENTOR(S): Linz, Guenter; Himmelsbach, Frank; Pieper, Helmut; Austel, Volkhard; Guth, Brian; Weisenberger, Johannes
PATENT ASSIGNEE(S): Dr. Karl Thomae Gmbh, Germany
SOURCE: Ger. Offen., 33 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19539091	A1	19970424	DE 1995-19539091	19951020
DE 19548798	A1	19970703	DE 1995-19548798	19951227
WO 9715567	A1	19970501	WO 1996-EP4390	19961010
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2229617	AA	19970501	CA 1996-2229617	19961010
EP 858457	A1	19980819	EP 1996-934603	19961010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11513382	T2	19991116	JP 1996-513786	19961010
US 5817677	A	19981006	US 1996-733898	19961018
PRIORITY APPLN. INFO.:			DE 1995-19539091	19951020
			DE 1995-19548798	19951227
			WO 1996-EP4390	19961010

GI



I II

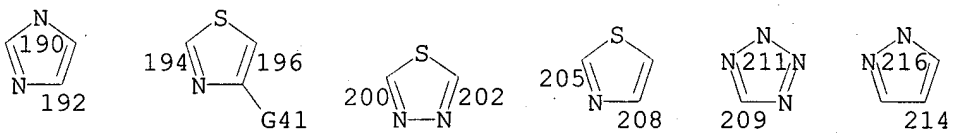
AB Five-membered heterocyclic compds., such as I [X = CMe, N; R = trans-4-(2-carboxyethyl)cyclohexyl, 4-HO2CCH2C6H4] and II were prepd. Thus, II was obtained by amidating the imidazolecarboxylic acid and

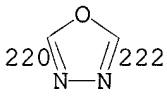
deprotection. II had IC50 in the fibrinogen binding test of 0.120 .mu.M and in the platelet aggregation inhibition test of 0.13 .mu.M.

MSTR 2

G3—G1—G16
2 3 4

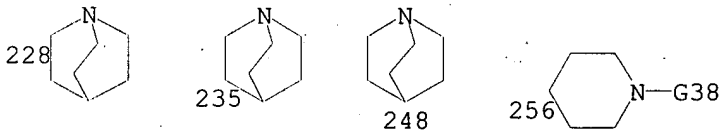
G1 = **Hy<EC (1-5) Q (-5) N (-2) S (-1) O (0) OTHERQ, RC (1), RS (1) E5> (SO (1-) G2)** /
Hy<EC (1-3) Q (-3) N (-2) S (-1) O (0) OTHERQ, AR (1-), BD (6) N, RC (2), RS (1) E5 (1) E6> (SO (1-) G2) /
(SC 190-2 192-4 / 194-2 196-4 / 200-2 202-4) /
(EX 205-2 208-4 / 211-2 209-4 / 216-2 214-4 / 220-2 222-4)





G2 = alkyl<(1-5)> / alkyl<(1-3)> (SR Ph) / Ph / pyridyl
G3 = cycloalkyl<(5-7)> (SO (1-) G9) / 225 / pyridyl / 228 / 235 / 248 / 224 / (SC 256)

G42—G8 G11—G12
224 1 225

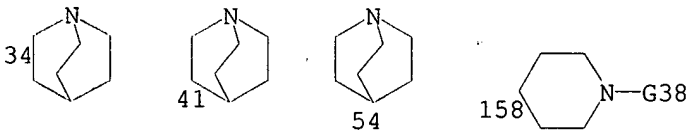


G4 = **O** / S
G5 = **(1-2) CH2**
G6 = C(O) / G5
G7 = H / alkyl<(1-3)> (SO Ph) / alkyl<(1-3)> (SR pyridyl) / (SC 175)

H2C—G39
175

G8 = cycloalkyl<(5-7)> (SO (1-) G9) / 19 / pyridyl / 34 / 41 / 54 / (SC 158)

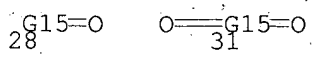
G11—G12
19



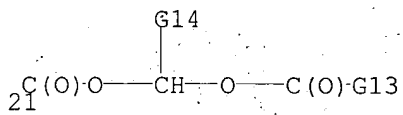
G9 = (-4) alkyl<(1-3)> / (-1) G10
G10 = OH / alkoxy<(1-3)> (SO Ph) / CN / CONH2 / **CO2H** /

alkoxycarbonyl<(1-3)> (SO Ph)

G11 = **Hy<EC (4-6) C (1) Q (1) N, AN (1-) C (1-) N, AR (0), BD (-1) DE (0) T, RC (1), RS (1) M5 (1) X7> (SO (1-) G9)** / Hy<EC (4-5) C (2) Q (2) N, AN (1-) N, AR (0), BD (ALL) S, RC (1), RS (1) M6 (1) X7> (SO (1-) G9) / 28 / 31



G12 = H / alkyl<(1-3)> (SO Ph) / alkoxycarbonyl<(1-5)> / alkoxycarbonyl<(1-3)> (SR Ph) / alkenyloxycarbonyl<(3-5)> / cycloalkyloxycarbonyl<(5-7)> / 21

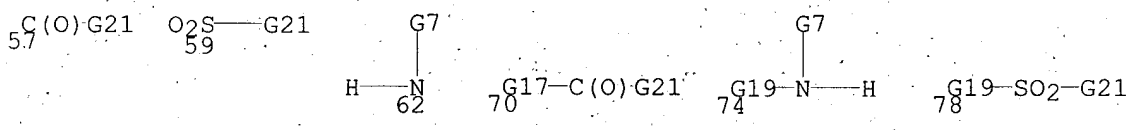


G13 = alkyl<(1-5)> / cycloalkyl<(5-7)> / alkyl<(1-3)> (SR Ph) / alkoxy<(1-5)> / cycloalkyloxy<(5-7)> / Ph

G14 = H / alkyl<(1-4)> / cycloalkyl<(5-7)> / Ph

G15 = Hy<EC (4-5) C (2) Q (2) N, AN (1-) C (1-) N, AR (0), BD (ALL) S, RC (1), RS (1) M6 (1) X7> (SO (1-) G9)

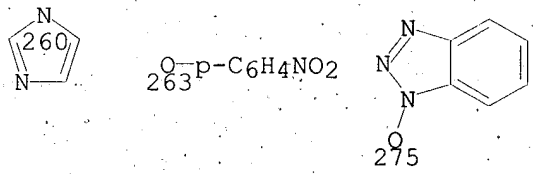
G16 = **57** / 59 / 70 / 78 / 62 / 74



G17 = alkylene<(1-3)> / alkenylene<(2-3)>

G19 = alkylene<(1-3)>

G21 = R<TX "leaving group"> / **(EX OH** / X / Cl / Br / 260 / 263 / 275)

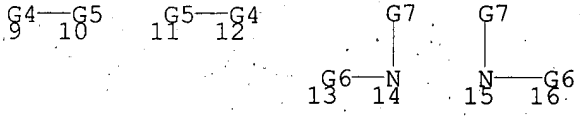


G38 = H / alkoxycarbonyl<(1-4)> / CO2CH2Ph

G39 = pyridyl

G41 = Me / (EX Ph / H)

G42 = alkylene<(1-8)> / alkenylene<(2-3)> / 9-1 10-3 / 11-1 12-3 / 13-1 14-3 / 15-1 16-3



MPL: claim 11

NTE: substitution is restricted

L3 ANSWER 39 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:330553 MARPAT
TITLE: Preparation of (guanidinophenyl)isoquinolinonecarboxyl ates, -naphthalenonecarboxylates, and related compounds as glycoprotein IIb/IIIa antagonists.
INVENTOR(S): Fisher, Matthew J.; Happ, Anne M.; Jakubowski, Joseph A.; Kinnick, Michael D.; Kline, Allen D.; Morin, Jr John M.; Sall, Daniel J.; Skelton, Marshall A.; Vasileff, Robert T.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 96,220, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5618843	A	19970408	US 1994-255821	19940708
IL 110172	A1	20011031	IL 1994-110172	19940630
TW 450953	B	20010821	TW 1994-83106357	19940713
AU 9467500	A1	19950202	AU 1994-67500	19940715
AU 685807	B2	19980129		
EP 635492	A1	19950125	EP 1994-305241	19940718
EP 635492	B1	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
ZA 9405251	A	19960118	ZA 1994-5251	19940718
AT 225337	E	20021015	AT 1994-305241	19940718
CA 2128348	AA	19950123	CA 1994-2128348	19940719
NO 9402734	A	19950123	NO 1994-2734	19940721
HU 70397	A2	19951030	HU 1994-2156	19940721
RU 2140907	C1	19991110	RU 1994-26092	19940721
PL 181905	B1	20011031	PL 1994-304388	19940721
FI 9403478	A	19950123	FI 1994-3478	19940722
BR 9402916	A	19950411	BR 1994-2916	19940722
CN 1108248	A	19950913	CN 1994-109191	19940722
CN 1057292	B	20001011		
JP 08188564	A2	19960723	JP 1994-170747	19940722
US 5731324	A	19980324	US 1995-376191	19950119
US 6137002	A	20001024	US 1996-710823	19960923
US 6020362	A	20000201	US 1998-47285	19980324
US 6472405	B1	20021029	US 1999-299404	19990426
CN 1274723	A	20001129	CN 1999-111888	19990731
FI 2000000648	A	20000320	FI 2000-648	20000320
US 6448269	B1	20020910	US 2001-883639	20010618

PRIORITY APPLN. INFO.:
US 1993-96220 19930722
US 1994-255821 19940708
US 1995-376191 19950119
US 1996-710823 19960923
US 1998-47285 19980324
US 1999-412142 19991005

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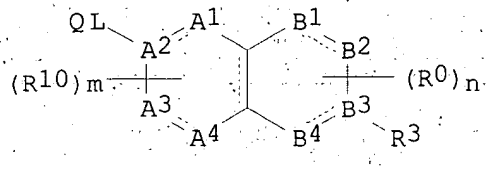
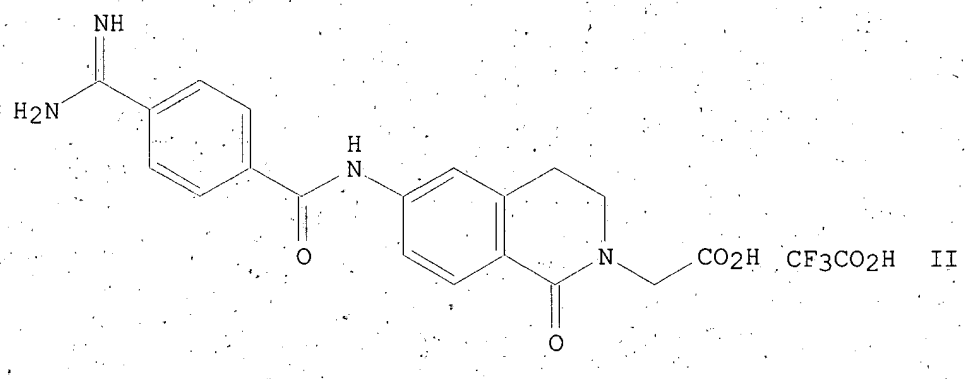


I

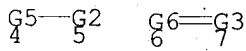


II

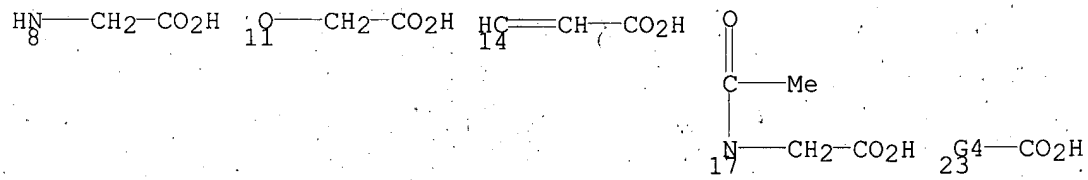
AB Title compds. [I; A1-A4, B1-B4 = C, O, S, N; .gtoreq.2 of A1-A4 and B1-B4 = C; L = bond, divalent (substituted) chain of 1-10 atoms; Q = org. group contg. .gtoreq.1 basic group; R3 = acidic group or salt, solvate, or prodrug thereof; R0, R10 = H, alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, OH, alkoxy, aralkoxy, amino, carbamyl, CO2H, acyl, cyano, halo, NO2, sulfo; m, n = 2-6], were prepd. Thus, title compd. (II) (multistep prepn. given) inhibited ADP-induced platelet aggregation with IC50 = 0.1 .mu.M.

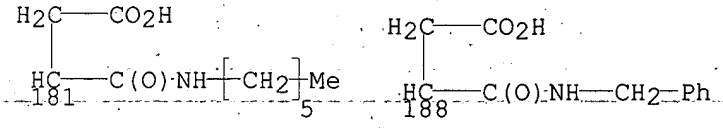
MSTR 2

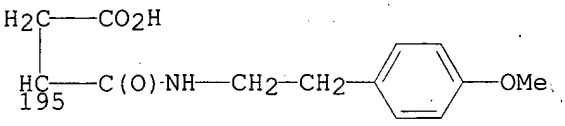
G1 = 4 / 6

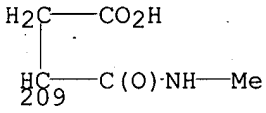


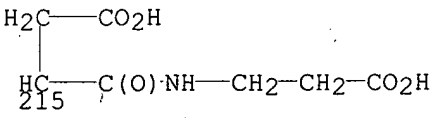
G2 = R<TX "acidic group"> / (EX CH2CO2H / 8 / 11 / CH2CH2CO2H / 14 / 17 / 23 / **CO2H** / 181 / 188 / 195 / 209 / 215 / 223 / 230 / 237 / 245 / 253 / 259 / 265 / 292 / 340)

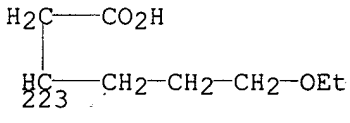


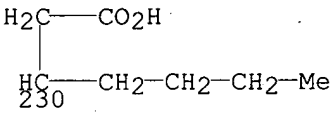


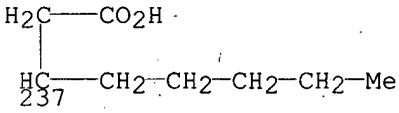


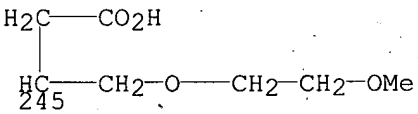


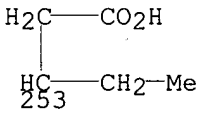


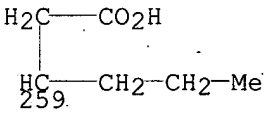


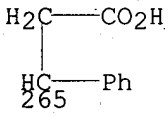


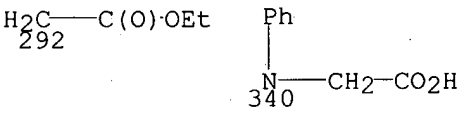




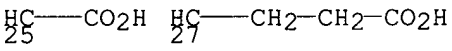




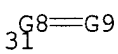


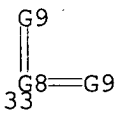


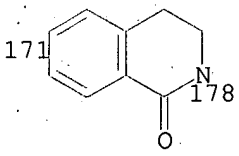
G3 = R<TX "acidic group"> / (EX 25 / 27)

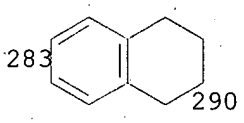


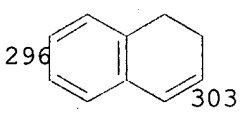
G4 = phenylene
G5 = **Cb<EC (10) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G7)** / Hy<EC (10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G7) / 31 / 33 / (EX 171-2 178-5 / 283-2 290-5 / 296-2 303-5 / 306-2 313-5 / 328-2 335-5 / 345-2 352-5 / 355-2 362-5)

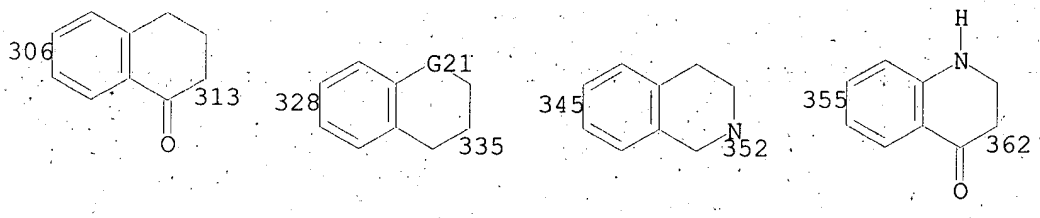




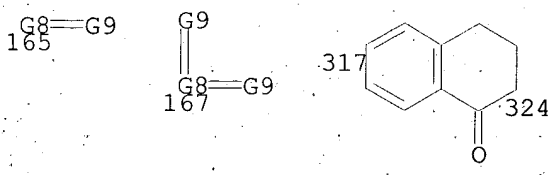




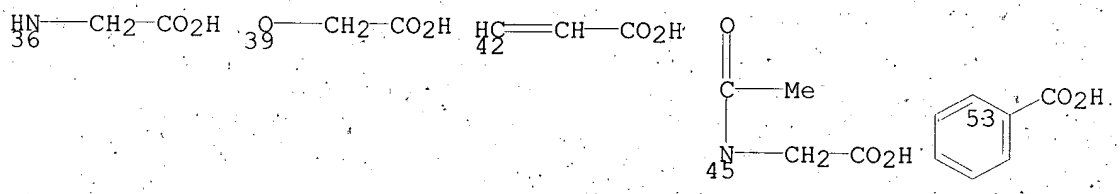


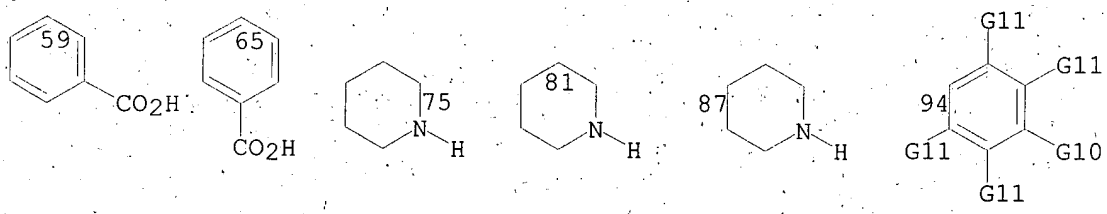


G6 = Cb<EC (10) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G7) / Hy<EC (10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G7) / 165 / 167 / (EX 317-2 324-7)



G7 = alkyl<(1-10)> (SO (1-) G22) / alkenyl<EC (2-10) C, BD (1) D> / alkynyl<(2-10)> / cycloalkyl<(3-10)> / aryl<RC (1-)> (SO) / alkyl<(1-6)> (SR (1-3) G23) / OH / alkoxy<(1-10)> / alkoxy<(1-6)> (SR (1-3) G23) / CO2H / acyl / CN / F / Cl / Br / I / NO2 / SO3H / R<TX "acidic or basic group"> / NH2 (SO) / CONH2 / (EX CH2CO2H / 36 / 39 / CH2CH2CO2H / 42 / 45 / 53 / 59 / 65 / CO2H / piperidino / 75 / 81 / 87 / NHC(NH)NH2 / C(NH)NH2 / 94)

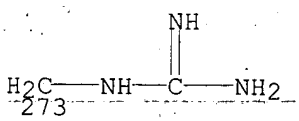




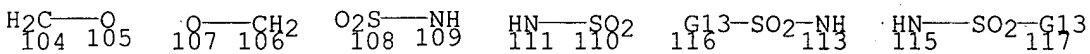
G8 = Cb<EC (10) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G7) / Hy<EC (10) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G7)

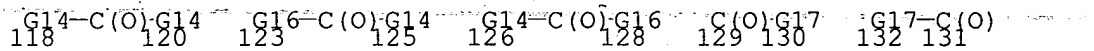
G9 = O / S

G10 = R<TX "basic radical"> / C(NH)NH2 / 273



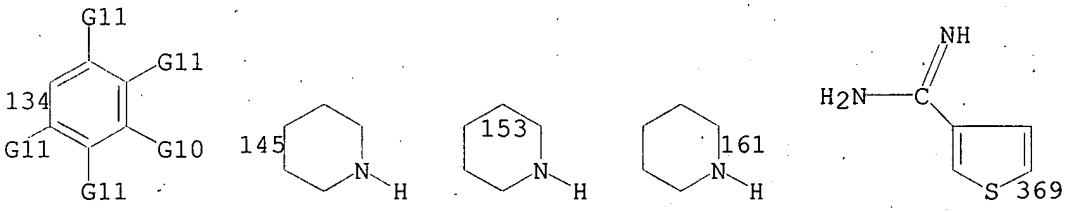
G11 = H / R
G12 = NULL / R<TX "linking group"> / (EX 104-1 105-3 / **107-1 106-3** / 108-1 109-3 / 111-1 110-3 / 116-1 113-3 / 115-1 117-3 / 118-1 120-3 / 123-1 125-3 / 126-1 128-3 / 129-1 130-3 / 132-1 131-3 / ethynylene / CH=CH / CH2CH2 / 270-1 272-3 / 278-1 281-3)



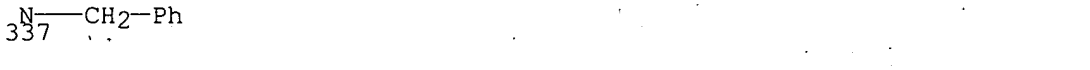


G13 = alkylene<(1-10)>
G14 = NH / 121

G15 = alkyl<(1-10)>
G16 = O / S
G17 = O / NH
G18 = R<TX "basic group"> / (EX 134 / 145 / 153 / 161 / **Cb<EC (6) C, RC (1), RS (1) E6> (SR (1-) G19)** / Hy<EC (6) A (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) E6> (SR (1-) G19) / 369)



G19 = (1-3) G20 / alkyl<(1-10)> (SO (1-) G22) / alkenyl<EC (2-6) C, BD (1) D> / alkynyl / cycloalkyl / aryl<RC (1-)> (SO) / alkyl<(1-10)> (SR (1-3) G23) / OH / alkoxy<(1-10)> / alkoxy<(1-10)> (SR (1-3) G23) / NH2 (SO) / CONH2 / **CO2H** / acyl / CN / F / Cl / Br / I / NO2 / SO3H
G20 = R<TX "basic group"> / NH2 / NHC(NH)NH2 / C(NH)NH2
G21 = O / NH / 337



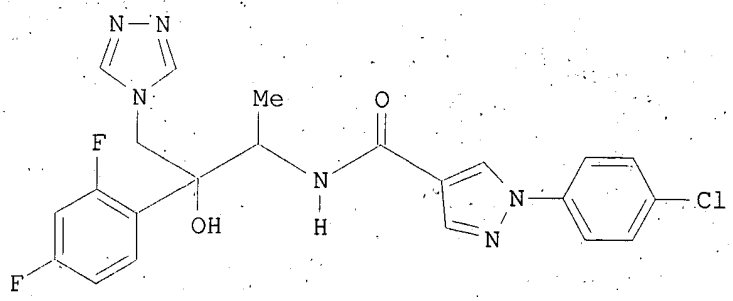
G22 = F / Cl / Br / I
G23 = aryl<RC (1-)> (SO)
DER: or pharmaceutically acceptable salts, solvates or prodrug derivatives
MPL: disclosure
NTE: substitution is restricted

L3 ANSWER 40 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:212156 MARPAT
TITLE: Preparation of heteroarylcarboxamides as agrochemical and medical fungicides
INVENTOR(S): Bartroli, Javier; Turmo, Enric; Anguita, Manuel
PATENT ASSIGNEE(S): J. Uriach & Cia. S.A., Spain; Bartroli, Javier; Turmo, Enric; Anguita, Manuel
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9705131	A1	19970213	WO 1996-EP3419	19960802
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
ES 2107376	A1	19971116	ES 1995-1564	19950802
ES 2107376	B1	19980701		
BR 9606546	A	19980714	BR 1996-6546	19950802
ES 2112774	A1	19980401	ES 1995-2042	19951020
ES 2112774	B1	19990516		
CA 2201478	AA	19970213	CA 1996-2201478	19960802
AU 9667889	A1	19970226	AU 1996-67889	19960802
EP 783502	A1	19970716	EP 1996-928404	19960802
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10507205	T2	19980714	JP 1996-507253	19960802
US 5888941	A	19990330	US 1997-809815	19970331
NO 9701471	A	19970530	NO 1997-1471	19970401

PRIORITY APPLN. INFO.: ES 1995-1564 19950802
ES 1995-2042 19951020
WO 1996-EP3419 19960802

GI

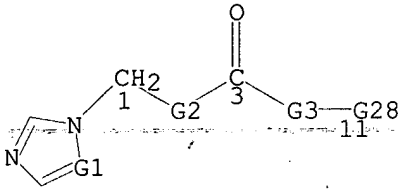


II

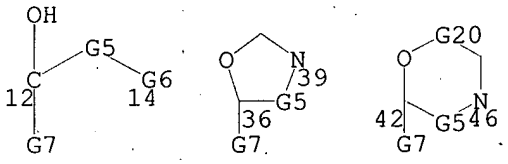
AB RCH2CR5(OR4)CR1R2NR3COZ1(CH2)mZ2(CH2)qR6 [I; R = imidazolo or 1,2,4-triazo-1-yl; R1 = alkyl; R2 = H or alkyl; R1R2 = alkylene; R3 = H (halo)alkyl, Ph, etc.; R4 = H; R3R4 = CH2, CH2CH2, CH(OH)CH2, COCH2; R5 = (halo- or CF3-substituted) Ph; R6 = (un)substituted Ph, -heterocyclyl; Z1 = (un)substituted phenylene or -heterocyclyene; Z2 = bond, O, SO0-2, NR6;

m,q = 0-2] were prepd. Thus, (2R,3R)-3-amino-2-(2,4-difluorophenyl)-1-(1H-1,2,4-triazol-1-yl)-2-butanol was amidated by 1-(4-chlorophenyl)-1H-pyrazole-4-carboxylic acid (prepn. given) to give title compd. (R,R)-II. Data for biol. activity of I were given.

MSTR 1



G1 = N / CH
G2 = 12-1 14-3 / 36-1 39-3 / 42-1 46-3



G3 = phenylene (SO (1-4) G36) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2),
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-4) G36) / 166-3 167-11 /
(SC 178-3 177-11 / 185-3 188-11 / 192-3 194-11 /
200-3 201-11 / 208-3 211-11 / 214-3 217-11 / 222-3 223-11 /
229-3 231-11 / 239-3 238-11 / 247-3 245-11 / 255-3 257-11 /
263-3 261-11 / 271-3 270-11 / 280-3 277-11 / 287-3 284-11 /
294-3 292-11 / 297-3 298-11 / 303-3 305-11 / 312-3 315-11 /
318-3 319-11 / 325-3 328-11 / 331-3 330-11 / 338-3 339-11 /
347-3 345-11 / 355-3 354-11 / 364-3 361-11 / 370-3 368-11 /
376-3 375-11 / 380-3 381-11 / 386-3 388-11 / 393-3 396-11 /
400-3 401-11 / 408-3 410-11 / 414-3 413-11 / 421-3 423-11 /
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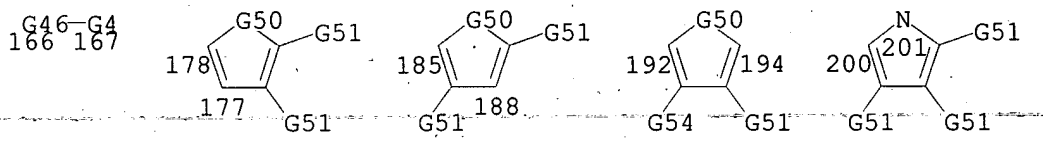
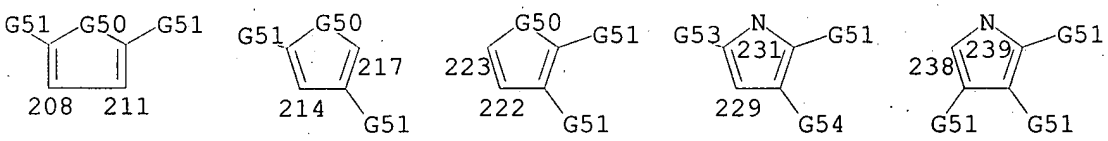
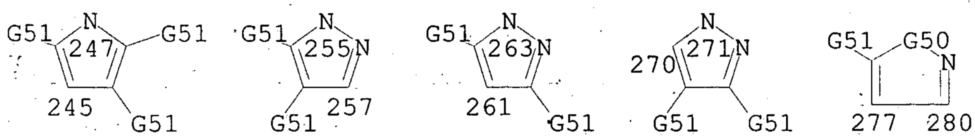
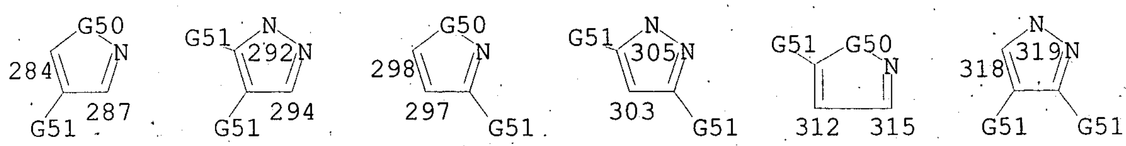
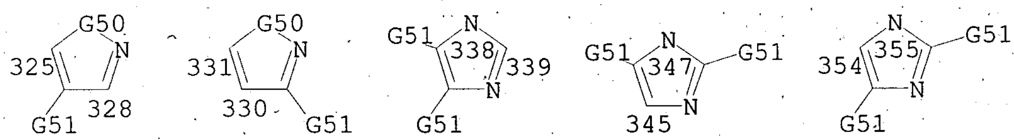
449-3 452-11 / 454-3 456-11)

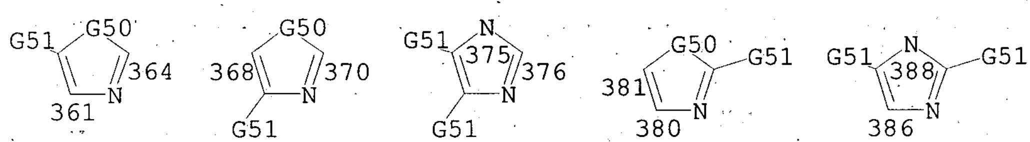


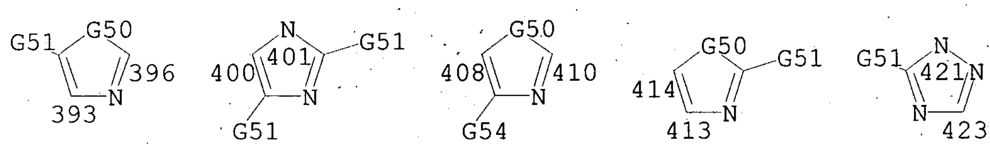


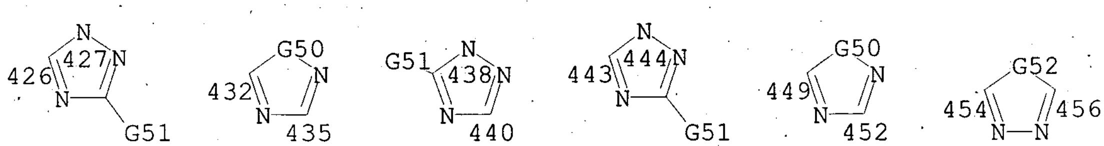




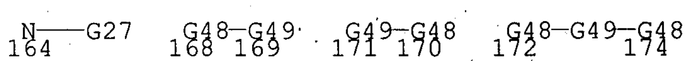




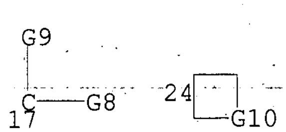




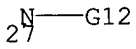
G4 = S / S(O) / SO2 / O / NH / 164 / G47 /
168-166 169-11 / 171-166 170-11 / 172-166 174-11



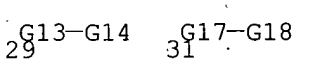
G5 = 17 / 24



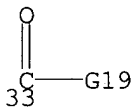
G6 = NH / 27



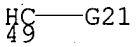
G7 = Ph (SO (1-) G11)
G8 = alkyl<(1-4)> / (SC Me)
G9 = H / alkyl<(1-4)>
G10 = (0-2) CH2
G11 = F / Cl / Br / I / CF3
G12 = alkyl<(1-4)> (SO (1-) G15) / cyclopropyl / cyclobutyl / cyclopentyl / cyclohexyl / 29 / 31



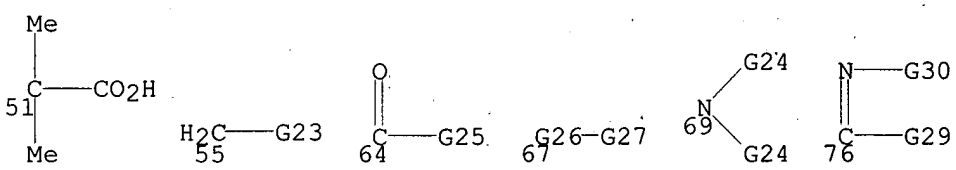
G13 = alkylene<(1-4)>
G14 = cyclopropyl / cyclobutyl / cyclopentyl / cyclohexyl / Ph (SO (1-) G16)
G15 = F / Cl / Br / I
G16 = alkyl<(1-4)> (SO (1-) G15) / F / Cl / Br / I
G17 = (1-4) CH2
G18 = OH / OCH2Ph / NH2 / alkylamino<(1-4)> / dialkylamino<(1-4)> / 33



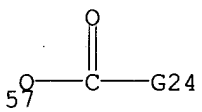
G19 = OH / alkoxy<(1-4)> / OCH2Ph
G20 = C(O) / 49



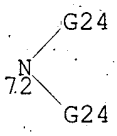
G21 = H / OH
G22 = alkyl<(1-4)> (SO (1-) G15) / alkenyl<(2-4)> / alkynyl<(2-4)> / cyclopropyl / cyclobutyl / cyclopentyl / cyclohexyl / alkoxy<(1-4)> (SO (1-) G15) / 51 / F / Cl / Br / I / NO2 / CN / OH / OCH2Ph / 55 / **64** / 67 / 69 / 76 / (-1) G55 / (SC CF3 / OCF3)



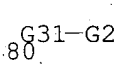
G23 = OH / 57



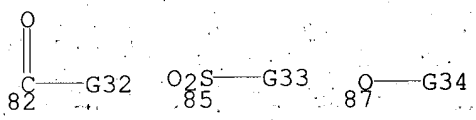
G24 = H / alkyl<(1-4)>
G25 = H / alkyl<(1-4)> / **OH** / alkoxy<(1-4)> / 72



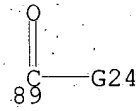
G26 = S / S(O) / SO2
G27 = alkyl<(1-4)>
G28 = **Ph (SO (1-4) G22)** / Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2), RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-4) G22)
G29 = NH2 / OH / 80



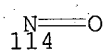
G30 = H / 82 / CN / 85 / OH / 87



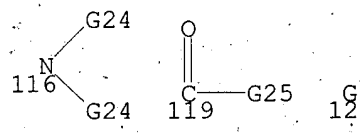
G31 = O / NH
G32 = NH2 / Me
G33 = NH2 / alkylamino<(1-4)> / alkyl<(1-4)>
G34 = alkyl<(1-4)> / 89



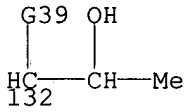
G35 = N / 114



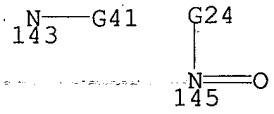
G36 = alkyl<(1-4)> (SO (1-) G15) / cyclopropyl / cyclobutyl / cyclopentyl / cyclohexyl / alkoxy<(1-4)> (SO (1-) G15) / F / Cl / Br / I / Ph (SO) / NO2 / CN / OH / CH2OH / 116 / **119** / 122



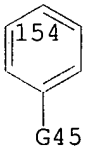
G37 = H / Me
G38 = H / Pr-i / cyclopentyl / cyclopropyl / Bu-s / CH2CH2CHMe2 / 132



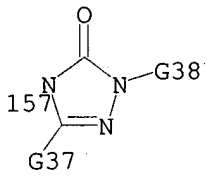
G39 = Me / Et
G40 = 143 / 145



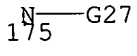
G41 = H / alkyl<(1-4)> / 154



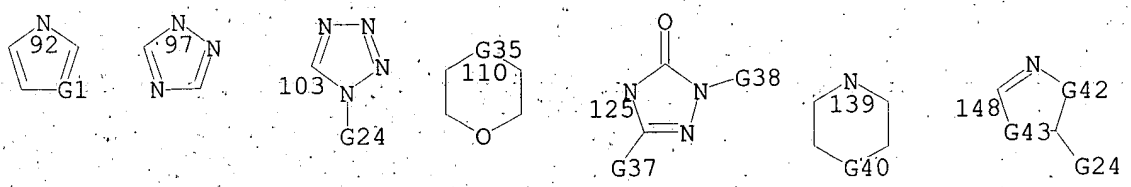
G42 = CH2 / C(O)
G43 = NH / O
G45 = F / Cl / Br / I / alkyl<(1-4)> (SR (1-) G15) /
alkoxy<(1-4)> (SR (1-) G15) / NO2 / NH2 / CN / 157



G46 = phenylene (SO (1-4) G36) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2),
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-4) G36)
G47 = (1-4) CH2
G48 = **(1-2) CH2**
G49 = S / S(O) / SO2 / O / NH / 175

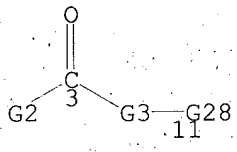


G50 = O / S / NH (SO)
G51 = H / R
G52 = O / S
G53 = H / R / (SC Me / CF3)
G54 = H / R / (SC Me)
G55 = 92 / 97 / 103 / pyrrolidino / 110 / Ph (SO) /
OPh (SO) / 125 / 139 / 148

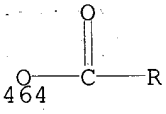


DER: and salts and solvates
MPL: claim 1

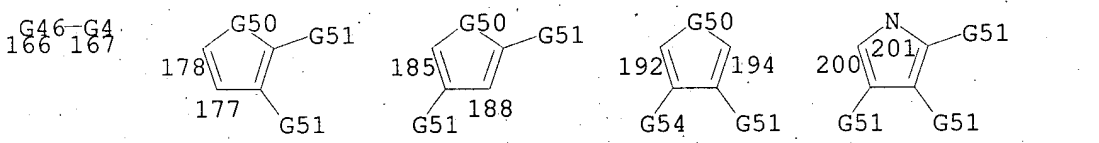
MSTR 3

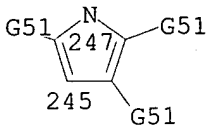


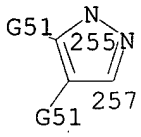
G1 = N / CH
G2 = **OH** / R<TX "reactive derivative"> / Cl / 464

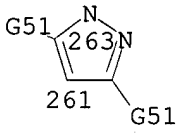


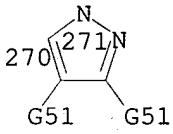
G3 = phenylene (SO (1-4) G36) /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2),
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-4) G36) / 166-3 167-11 /
(SC 178-3 177-11 / 185-3 188-11 / 192-3 194-11 /
200-3 201-11 / 208-3 211-11 / 214-3 217-11 / 222-3 223-11 /
229-3 231-11 / 239-3 238-11 / 247-3 245-11 / 255-3 257-11 /
263-3 261-11 / 271-3 270-11 / 280-3 277-11 / 287-3 284-11 /
294-3 292-11 / 297-3 298-11 / 303-3 305-11 / 312-3 315-11 /
318-3 319-11 / 325-3 328-11 / 331-3 330-11 / 338-3 339-11 /
347-3 345-11 / 355-3 354-11 / 364-3 361-11 / 370-3 368-11 /
376-3 375-11 / 380-3 381-11 / 386-3 388-11 / 393-3 396-11 /
400-3 401-11 / 408-3 410-11 / 414-3 413-11 / 421-3 423-11 /
427-3 426-11 / 435-3 432-11 / 440-3 438-11 / 443-3 444-11 /
449-3 452-11 / 454-3 456-11)

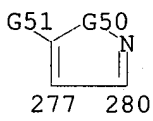


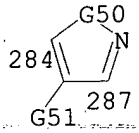


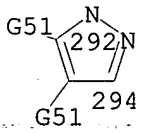


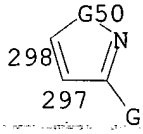


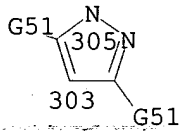


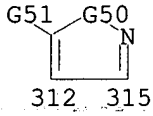


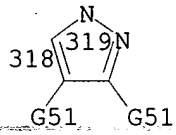


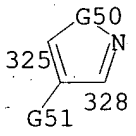


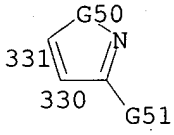


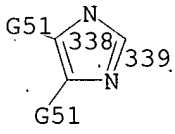


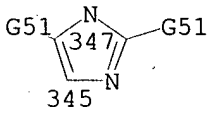


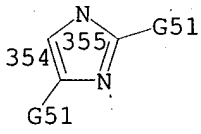


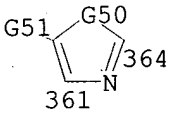


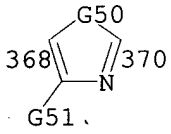


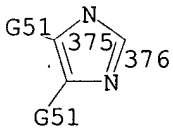


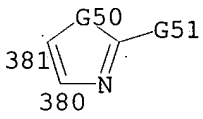


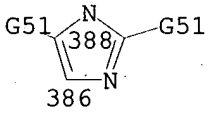


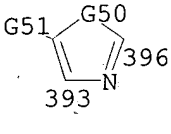


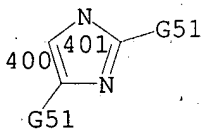


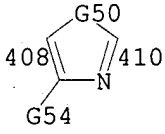


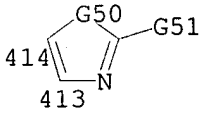


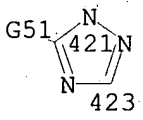


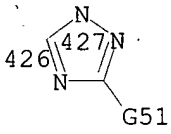


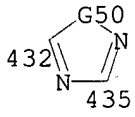


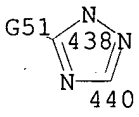


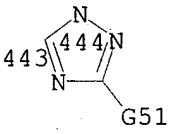


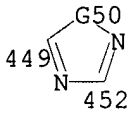


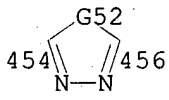








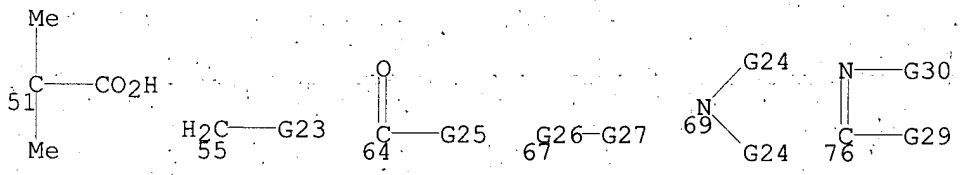




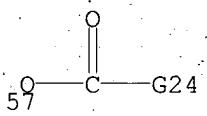
G4 = S / S(O) / SO2 / O / NH / 164 / G47 /
168-166 169-11 / 171-166 170-11 / 172-166 174-11

N——G27 G48—G49 G49—G48 G48—G49—G48
164 168 169 171 170 172 174

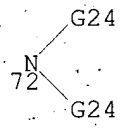
G15 = F / Cl / Br / I
G22 = alkyl<(1-4)> (SO (1-) G15) / alkenyl<(2-4)> /
alkynyl<(2-4)> / cyclopropyl / cyclobutyl / cyclopentyl /
cyclohexyl / alkoxy<(1-4)> (SO (1-) G15) / 51 / F / Cl / Br /
I / NO2 / CN / OH / OCH2Ph / 55 / **64** / 67 / 69 / 76 /
(-1) G55 / (SC CF3 / OCF3)



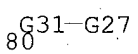
G23 = OH / 57



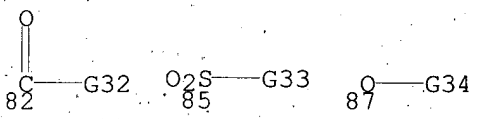
G24 = H / alkyl<(1-4)>
G25 = H / alkyl<(1-4)> / **OH** / alkoxy<(1-4)> / 72



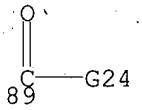
G26 = S / S(O) / SO2
G27 = alkyl<(1-4)>
G28 = **Ph (SO (1-4) G22)** / Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2), RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-4) G22)
G29 = NH2 / OH / 80



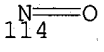
G30 = H / 82 / CN / 85 / OH / 87



G31 = O / NH
G32 = NH2 / Me
G33 = NH2 / alkylamino<(1-4)> / alkyl<(1-4)>
G34 = alkyl<(1-4)> / 89

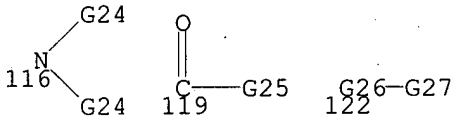


G35 = N / 114

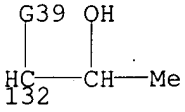


G36 = alkyl<(1-4)> (SO (1-) G15) / cyclopropyl /

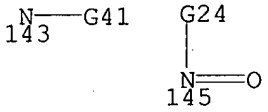
cyclobutyl / cyclopentyl / cyclohexyl /
alkoxy<(1-4)> (SO (1-) G15) / F / Cl / Br / I / Ph (SO) /
NO2 / CN / OH / CH2OH / 116 / 119 / 122



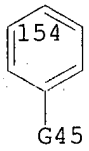
G37 = H / Me
G38 = H / Pr-i / cyclopentyl / cyclopropyl / Bu-s /
CH2CH2CHMe2 / 132



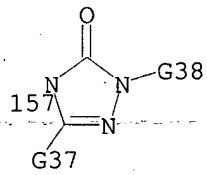
G39 = Me / Et
G40 = 143 / 145



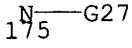
G41 = H / alkyl<(1-4)> / 154



G42 = CH2 / C(O)
G43 = NH / O
G45 = F / Cl / Br / I / alkyl<(1-4)> (SR (1-) G15) /
alkoxy<(1-4)> (SR (1-) G15) / NO2 / NH2 / CN / 157

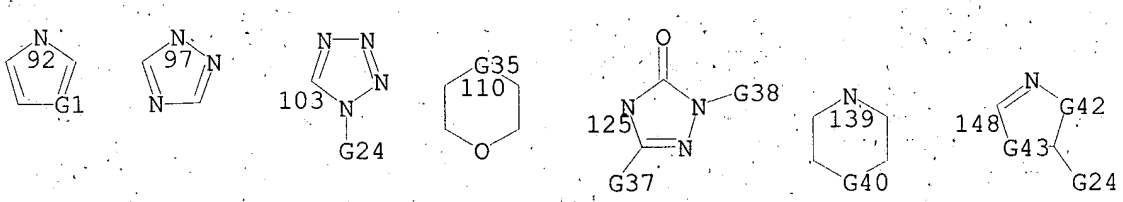


G46 = **phenylene (SO (1-4) G36)** /
Hy<EC (1-4) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2),
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-4) G36)
G47 = (1-4) CH2
G48 = **(1-2) CH2**
G49 = S / S(O) / SO2 / O / NH / 175



G50 = O / S / NH (SO)

G51 = H / R
G52 = O / S
G53 = H / R / (SC Me / CF3)
G54 = H / R / (SC Me)
G55 = 92 / 97 / 103 / pyrrolidino / 110 / Ph (SO) / OPh (SO) / 125 / 139 / 148



MPL: claim 14

L3 ANSWER 41 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:171490 MARPAT
TITLE: Preparation of 2-pyridinones as thrombin inhibitors
INVENTOR(S): Sanderson, Philip E.; Naylor-Olsen, Adel M.; Dyer, Dona L.; Vacca, Joseph P.; Isaacs, Richard C. A.; Dorsey, Bruce D.; Fraley, Mark E.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Sanderson, Philip E.; Naylor-Olsen, Adel M.; Dyer, Dona L.; Vacca, Josep, P.; Isaacs, Richard C. A.; Dorsey, Bruce D.; Fraley, Mark, E.
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9701338	A1	19970116	WO 1996-US10778	19960624
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2224437	AA	19970116	CA 1996-2224437	19960624
AU 9663917	A1	19970130	AU 1996-63917	19960624
AU 703744	B2	19990401		
EP 835109	A1	19980415	EP 1996-923399	19960624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11508558	T2	19990727	JP 1996-504499	19960624

PRIORITY APPLN. INFO.: US 1995-560P 19950627
US 1995-3818P 19950915
GB 1996-3450 19960219
WO 1996-US10778 19960624

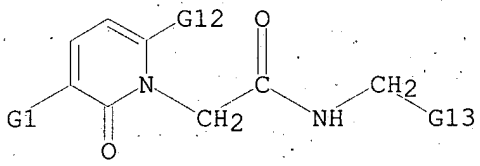
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

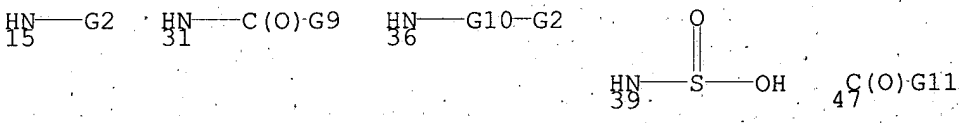
AB The title compds. [I; W = benzenemethylsulfonyl, diphenylmethylsulfonyl,

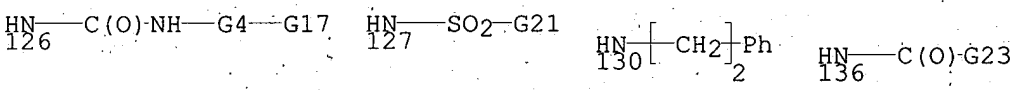
naphthylsulfonyl, etc.; A = trans-4-aminocyclohexyl, 2-aminopyridin-4-yl, etc.; R3 = H, C1-4 alkyl, C3-7 cycloalkyl, CF3], useful in inhibiting thrombin and assocd. thrombotic occlusions, were prepd. Thus, reaction of PhCH2SO2Cl with 2-pyridinone II in the presence of Et3N in CH2Cl2 followed by treatment of the intermediate III in CH2Cl2/EtOAc with HCl gas, reaction of the Boc-deprotected intermediate with H2NC(:NH)SO3H in the presence of Et3N in DMF, and treatment of the resulting 2-pyridinone IV in MeOH/THF with 1M LiOH afforded V which showed Ki < 100 nM against human thrombin and Ki of > 500 nM against human trypsin.

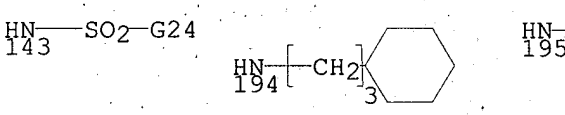
MSTR 1

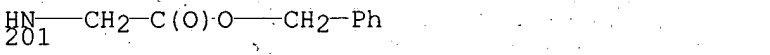


G1 = NH2 / 15 / 31 / NHCHO / 36 / 39 / 47 / 126 / (SC 127 / 130) / (EX 136 / 143 / 194 / 195 / 201)

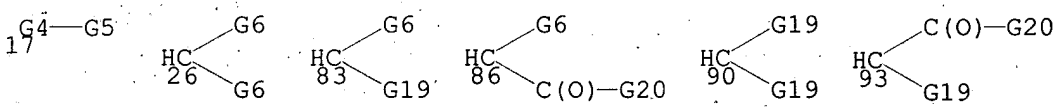


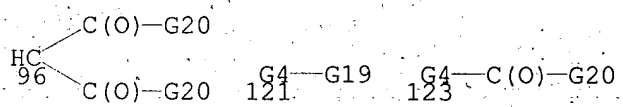




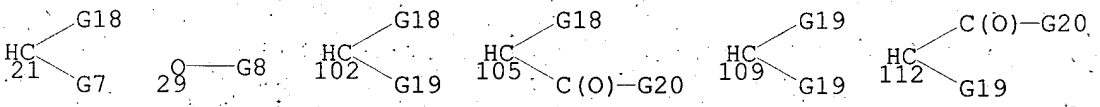


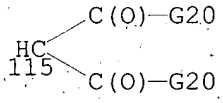
G2 = Ph (SO (1-) G3) / naphthyl / biphenylyl / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> / Hy<EC (9-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (2)> / CO2H / alkoxycarbonyl<(1-4)> / alkyl<(1-4)> / cycloalkyl<(3-7)> / cycloalkyl<EC (7-12) C, RC (2)> / 17 / 26 / 83 / 86 / 90 / 93 / 96 / 121 / 123



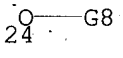


G3 = alkyl<(1-4)> / alkoxy<(1-4)> / F / Cl / Br / I / CF3 / OH / **CO2H** / CONH2
G4 = alkylene<EC (1-4) C, DC (0) M3>
G5 = H / Ph (SO (1-) G3) / naphthyl / biphenylyl / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> / Hy<EC (9-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (2)> / cycloalkyl<(3-7)> / cycloalkyl<EC (7-12) C, RC (2)> / **21** / OH / 29 / 102 / 105 / 109 / 112 / 115

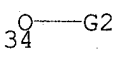




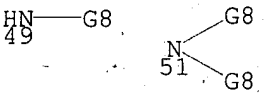
G6 = H / Ph (SO (1-) G3) / naphthyl / biphenylyl / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> / Hy<EC (9-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (2)> / cycloalkyl<(3-7)> / cycloalkyl<EC (7-12) C, RC (2)>
G7 = OH / **24** / H / Ph (SO (1-) G3) / naphthyl / biphenylyl / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> / Hy<EC (9-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (2)> / cycloalkyl<(3-7)> / cycloalkyl<EC (7-12) C, RC (2)>



G8 = **Ph (SO (1-) G3)** / naphthyl / biphenylyl / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> / Hy<EC (9-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (2)> / CO2H / alkoxycarbonyl<(1-4)> / alkyl<(1-4)> / cycloalkyl<(3-7)> / cycloalkyl<EC (7-12) C, RC (2)>
G9 = OH / 34

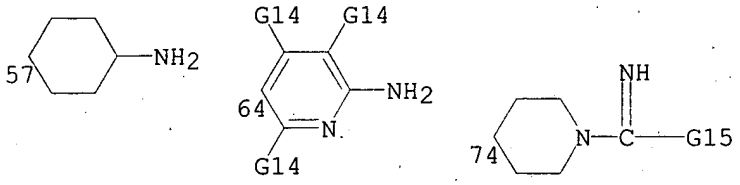


G10 = C(O) / SO2
G11 = NH2 / 49 / 51

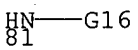


G12 = H / alkyl<(1-4)> / cycloalkyl<(3-7)> / CF3 / (SC Me)

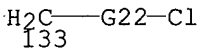
G13 = 57 / 64 / 74



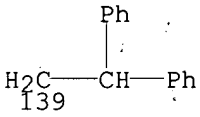
G14 = (1-) H / alkyl<(1-4)> / alkoxy<(1-4)> / cycloalkyl<(3-7)> / F / Cl / Br / I / CF3 / (SC Me)
G15 = NH2 / 81



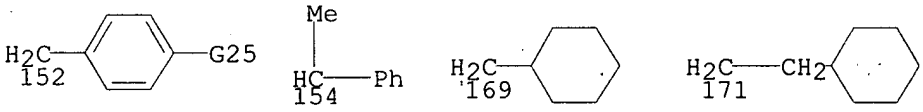
G16 = OH / CN
G17 = H / Ph (SO (1-) G3) / naphthyl / biphenylyl / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> / Hy<EC (9-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (2)> / CO2H / alkoxycarbonyl<(1-4)> / alkyl<(1-4)> / cycloalkyl<(3-7)> / cycloalkyl<EC (7-12) C, RC (2)>
G18 = H / **Ph (SO (1-) G3)** / naphthyl / biphenylyl / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> / Hy<EC (9-10) A (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (2)> / cycloalkyl<(3-7)> / cycloalkyl<EC (7-12) C, RC (2)>
G19 = alkyl<(1-4)>
G20 = OH / alkoxy<(1-4)>
G21 = CH2Ph / CHPh2 / p-C6H4Me / 133

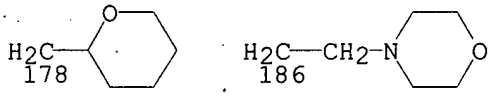


G22 = phenylene
G23 = OCH2Ph / CH2Ph / CH2CH2Ph / 139



G24 = 152 / 154 / 169 / 171 / 178 / Bu-n / CH2CH2CHMe2 / pentyl / 186





G25 = F / Br

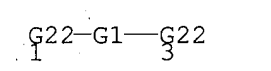
DER: and pharmaceutically acceptable salts
MPL: claim 1
STE: 57-trans

L3 ANSWER 42 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:60367 MARPAT
TITLE: Preparation of aryloxy- and arylthioglutamic acids as excitatory amino acid receptor antagonists
INVENTOR(S): Heinz, Lawrence J.; Lunn, William H. W.; Schoepp, Darryle D.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 31 pp., Cont.-in-part of U.S. Ser. No. 161,830,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

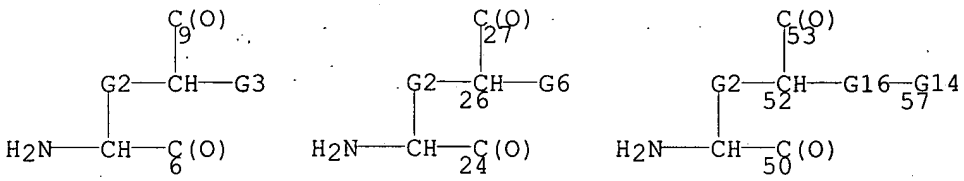
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5576323	A	19961119	US 1994-322632	19941013
ZA 9409405	A	19960528	ZA 1994-9405	19941128
NO 9404578	A	19950606	NO 1994-4578	19941129
AU 9479151	A1	19950608	AU 1994-79151	19941130
AU 676781	B2	19970320		
BR 9404809	A	19950801	BR 1994-4809	19941201
FI 9405704	A	19950604	FI 1994-5704	19941202
EP 658539	A1	19950621	EP 1994-308949	19941202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 69181	A2	19950828	HU 1994-3469	19941202
CN 1108240	A	19950913	CN 1994-119360	19941202
JP 07267908	A2	19951017	JP 1994-299390	19941202
US 5843997	A	19981201	US 1996-626447	19960402
PRIORITY APPLN. INFO.:			US 1993-161830	19931203
			US 1994-322632	19941013

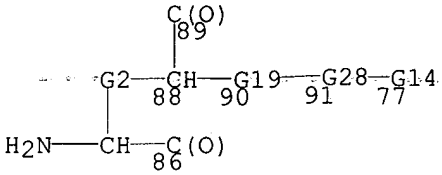
AB Novel compds. R3pX3mX2sX1nCH(CO2R2)(CH2)rCH(NH2)CO2R1 [R1, R2 = H, protective group, R3, X2 = (un)substituted aryl or heterocyclyl group, X1 = NH2 or substituted amino, O, S, X3 = alkylene, alkenediyl, oxoalkylene, oxyalkylene, etc., m, n, s = 0, 1, p = 0-3, q = 0-6, r = 1, 2] or their pharmaceutically acceptable salts were prepd. as antagonists of excitatory amino acid receptors. Thus, Me 3-hydroxy-2-pyrrolidone-5-carboxylate was prepd. in 4 steps from cyclopentadiene and benzyl N-hydroxycarbamate and etherified with phenol and treated with LiOH in H2O-THF to afford 4-phenoxyglutamic acid. The latter at 10 .mu.M concn. gave 88.0% displacement of 3H-glutamate binding from rat brain cell membranes. Formulation contg. the title compds. are given.

MSTR 1

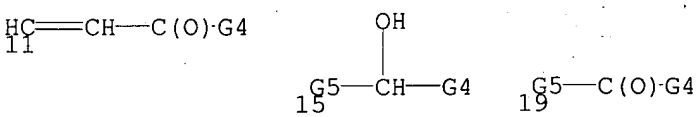


G1 = 6-1 9-3 / 24-1 27-3 / 50-1 53-3 / 86-1 89-3

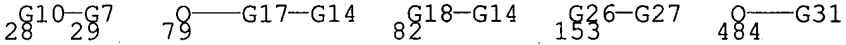




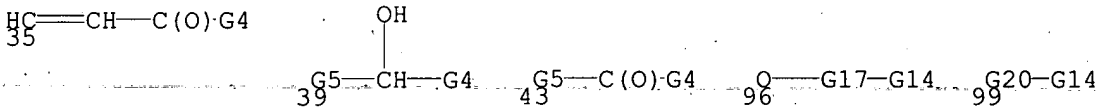
G2 = (1-2) CH2
G3 = 11 / 15 / 19

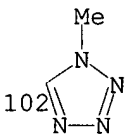


G4 = alkyl<(1-10)>
G5 = NULL / alkylene<EC (1-6) C, DC (0) M3>
G6 = 28 / aryl (SO (1-) G8) /
Hy<EC (1-8) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-) G9) / 79 / 82 /
(SC tetrazolyl / triazolyl / 153) / (EX 484)



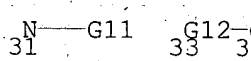
G7 = 35 / 39 / 43 / aryl (SO (1-) G8) /
Hy<EC (1-8) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-) G9) / 96 / 99 /
(SC Ph (SO (1-) G29) / naphthyl (SO) / pyrimidinyl / 102 /
pyridyl (SO))





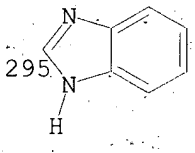
G8 = X / OH / CN / NO2 / alkyl<(1-10)> /
cycloalkyl<(3-6)> / alkoxy<(1-4)> / CO2H / COMe / CHO /
CH2CO2H / CH2OH / NH2 / CH2NH2 / CF3
G9 = X / OH / CN / NO2 / alkyl<(1-6)> / alkoxy<(1-4)> /
alkoxycarbonyl / **CO2H** / CH2CO2H / CH2OH / NH2 / CH2NH2 / CF3

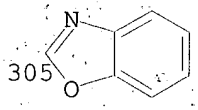
G10 = NH / 31 / O / S / arylene (SO (1-) G8) /
Hy<EC (1-8) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-) G9) / 33-26 34-29



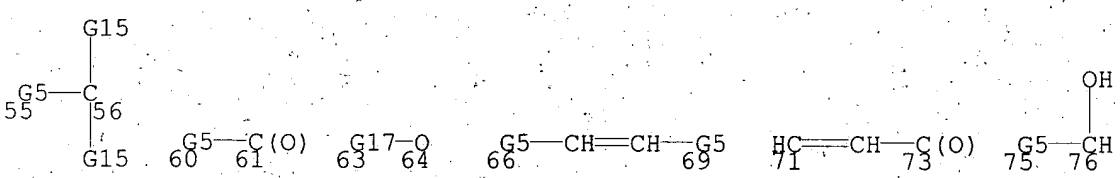
G11 = alkyl<(1-10)> / CHO / alkylcarbonyl<(1-6)> /
alkylsulfonyl<(1-4)>
G12 = NH / 46 / O / S

G13 = arylene (SO (1-) G8) /
Hy<EC (1-8) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-) G9) /
(SC phenylene (SO))
G14 = aryl (SO (1-) G8) / **Hy<EC (1-8) Q (0-) N (0-) O (0-)
S (0) OTHERQ, RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-) G9)** /
(SC Ph (SO (1-) G29) / pyridyl (SO)) / (EX 2-thiazolyl /
295 / 305)

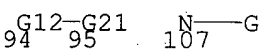




G15 = H / aryl (SO (1-) G8) /
Hy<EC (1-8) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-) G9) / (SC Ph (SO) /
pyridyl (SO))
G16 = 55-52 56-57 / 60-52 61-57 / 63-52 64-57 /
66-52 69-57 / 71-52 73-57 / 75-52 76-57

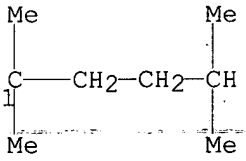


G17 = alkylene<EC (1-6) C, DC (0) M3>
G18 = S(O) / SO2
G19 = NH / 107 / O / S / arylene (SO (1-) G8) /
**Hy<EC (1-8) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-) G9)** / 94-88 95-91



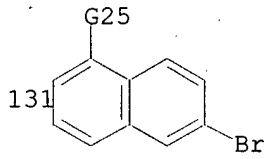
G20 = NH / 92 / O / S / S(O) / SO2

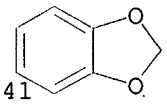
G21 = arylene (SO (1-) G8) /
Hy<EC (1-8) Q (0-) N (0-) O (0-) S (0) OTHERQ,
RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-) G9) /
(SC phenylene (SO))
G22 = OH (SO)
G23 = Me / OMe / Pr-i / cyclopentyl / 111 / COMe / CF3 /
Cl

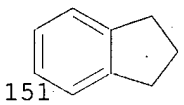


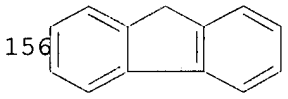
G24 = Me / Br
G25 = H / Br
G26 = O / S
G27 = 119 / 109 / 121 / naphthyl / 131 / 141 / 151 / 156 /
168 / 181 / 200 / 210

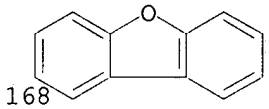
p-C6H4G23 109 o-C6H4G24 119 m-C6H4I 121

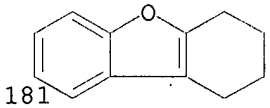


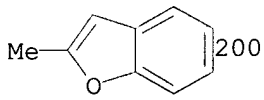


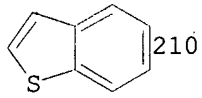




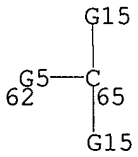


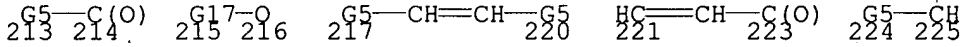


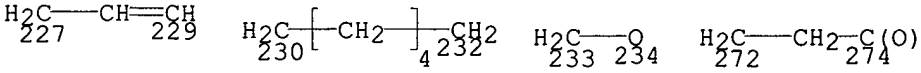




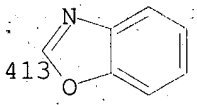
G28 = 62-90 65-77 / 213-90 214-77 / 215-90 216-77 /
217-90 220-77 / 221-90 223-77 / 224-90 225-77 / (SC CH2 /
CH2CH2CH2 / CH2CH2CH2CH2 / 227-90 229-77 / 230-90 232-77 /
233-90 234-77) / (EX CH2CH2 / 272-90 274-77)



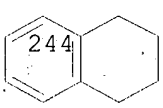


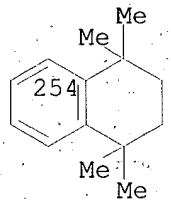


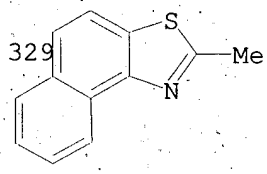
G29 = R / Cl / NO2
G30 = Ph / 413

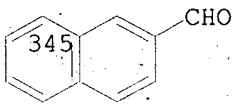


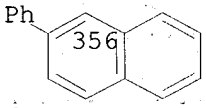
G31 = 510 / 244 / 254 / 529 / 329 / 345 / 356 / 364 / 378 / 391 / 407 / 430 / 452 / 464 / 468 / 474 / 487 / 493 / 503

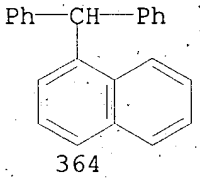


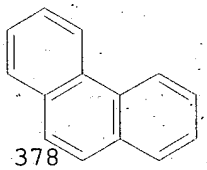


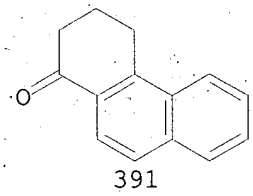


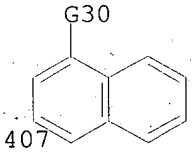


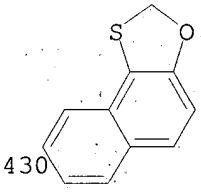


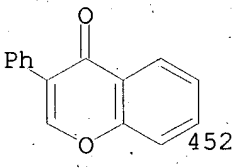


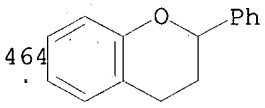


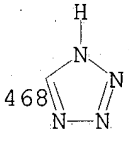


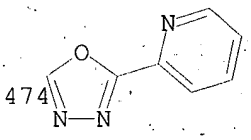


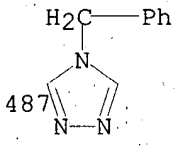


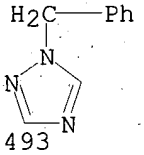


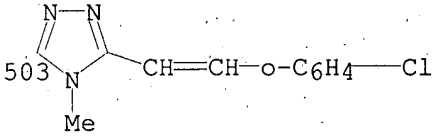


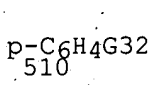


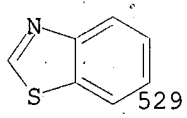




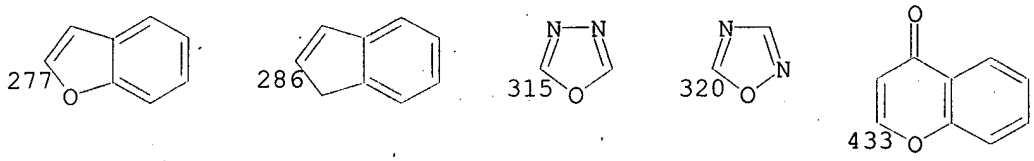


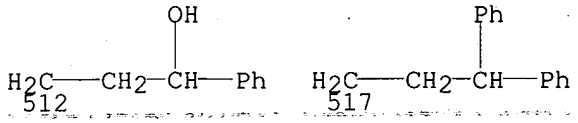






G32 = C(Me)2CH2CMe3 / morpholino / 277 / 286 / 315 / 320 / COMe / 433 / NHSO2Me / 512 / 517





DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted
NTE: additional ring fusion also claimed

L3 ANSWER 43 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:247613 MARPAT
TITLE: Preparation of indolines as 5-HT2B/2C receptor antagonists
INVENTOR(S): Gaster, Laramie Mary; Wyman, Paul Adrian; Mulholland, Keith Raymond; Davies, David Thomas; Duckworth, David Malcom; Forbes, Ian Thomson; Jones, Graham Elgin
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623783	A1	19960808	WO 1996-EP368	19960126
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
CA 2212061	AA	19960808	CA 1996-2212061	19960126
AU 9646646	A1	19960821	AU 1996-46646	19960126
AU 699727	B2	19981210		
BR 9607016	A	19971028	BR 1996-7016	19960126
EP 808312	A1	19971126	EP 1996-902259	19960126
EP 808312	B1	20001102		
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CN 1179156	A	19980415	CN 1996-192777	19960126
JP 10513442	T2	19981222	JP 1996-523247	19960126
RO 115522	B3	20000330	RO 1997-1439	19960126
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ES 2151652	T3	20010101	ES 1996-902259	19960126
PL 184490	B1	20021129	PL 1996-321706	19960126
ZA 9600758	A1	19970930	ZA 1996-758	19960131
IL 116998	A1	20010808	IL 1996-116998	19960201
FI 9703205	A	19971001	FI 1997-3205	19970801
NO 9703543	A	19971001	NO 1997-3543	19970801

US 5990133	A	19991123	US 1997-875506	19971016
US 6235758	B1	20010522	US 1999-359606	19990731
PRIORITY APPLN. INFO.:			GB 1995-2052	19950202
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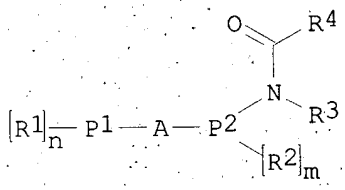
			WO 1996-EP368	19960126
			US 1997-875506	19971016

OTHER SOURCE(S): CASREACT 125:247613

GI



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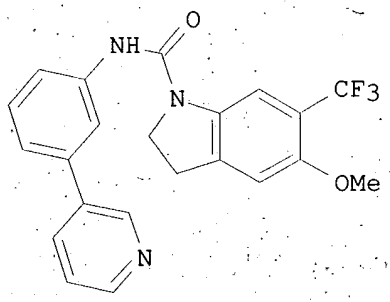
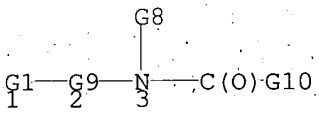


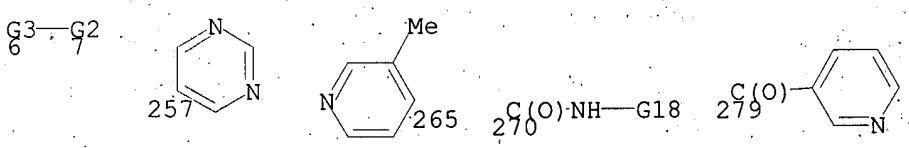
II

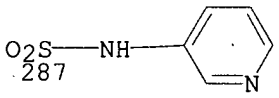
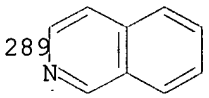
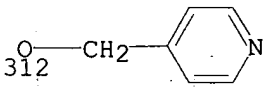
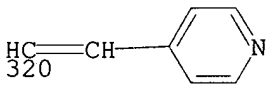
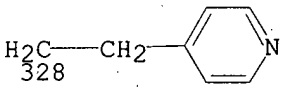
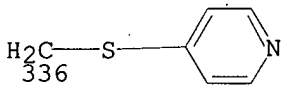
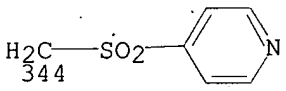
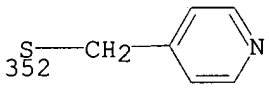
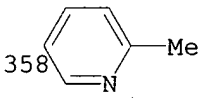
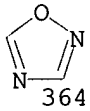
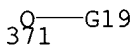
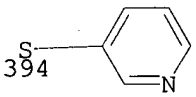
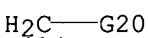
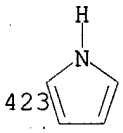
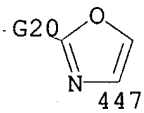
AB The title compds. [I; P1, P2 = Ph, arom. or partially satd. monocyclic or bicyclic heterocyclic ring; A = bond, (substituted) C1-5 alkylene, etc.; R1, R2 = H, (substituted) C1-6 alkyl, C2-6 alkenyl, etc.; R3 = H, C1-6 alkyl; R4 = 1-indolinyl, etc.; n, m = 0-2], useful in the treatment of CNS disorders such as anxiety, were prepd. Thus, treatment of 3-(3-pyridyl)aniline with 1,1-dicarbonyldiimidazole in CH2Cl2 followed by reaction of the intermediate with 5-methoxy-6-trifluoromethylindoline in DMF afforded 85% the indoline II which showed pKi of 5.8-9.7 against [3H]-mesulergine binding to rat or human 5-HT2C clones expressed in 293 cells in vitro.

MSTR 1



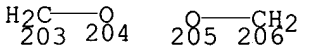
G1 = Ph (SO (-2) G4) / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO (-2) G4) / 6 / (SC pyridyl / 257 / 265 / 270 / 279 / 287 / 289 / 312 / 320 / 328 / 336 / 344 / 352 / 358 / 364 / 371 / 394 / pyrazinyl / 414 / thienyl / 423 / 2-furyl / 447)



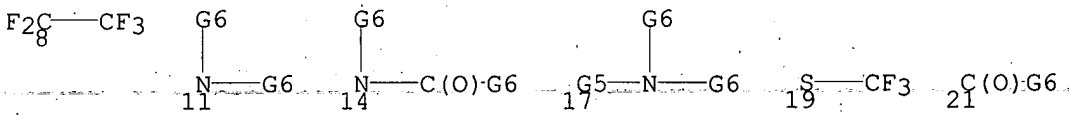
















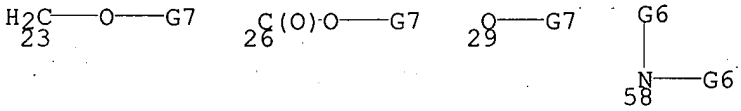
G2 = **Ph (SO (-2) G4)** / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO (-2) G4)

G3 = R<TX "chain of 1 to 5 atoms"> (SO alkyl<(1-6)>) / phenylene (SO) / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> (SO) / (SC 203-2 204-7 / **205-2 206-7** / O)



G4 = alkyl<(1-6)> (SO 58) / alkenyl<(2-6)> / alkynyl<(2-26)> / alkyl<(1-6)> / CN / NO2 / F / Cl / Br / I / CF3 / 8 / 11 / 14 / 17 / CHO / OCF3 / 19 / 21 / CH2OH / 23 / **CO2H** / 26 / OH / 29 / (SC Me)





G5 = S / S(O) / SO2

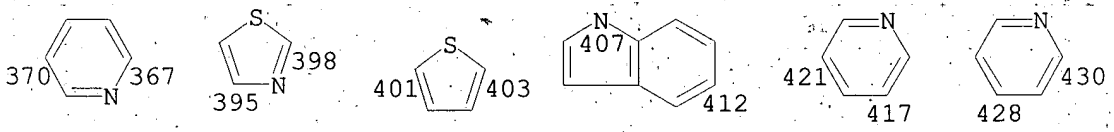
G6 = H / alkyl<(1-6)> / aryl (SO) / alkyl<(1-6)> (SR aryl)

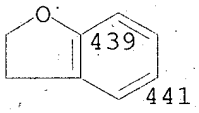
G7 = alkyl<(1-6)> / aryl (SO) / alkyl<(1-6)> (SR aryl)

G8 = H / alkyl<(1-6)>

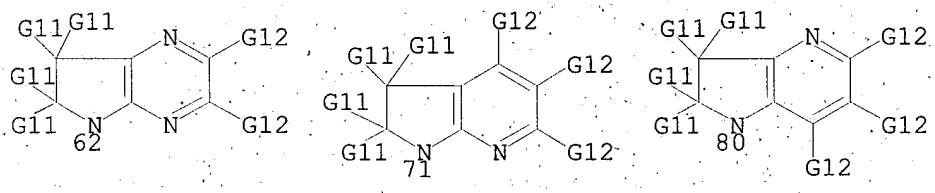
G9 = phenylene (SO (-2) G17) /

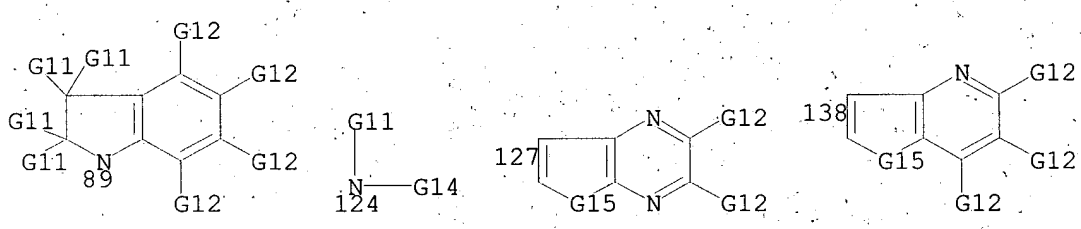
Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)>
(SO (-2) G17) / (SC 370-3 367-1 / 395-3 398-1 / 401-3 403-1 /
412-3 407-1 / 421-3 417-1 / 428-3 430-1 / 441-3 439-1)

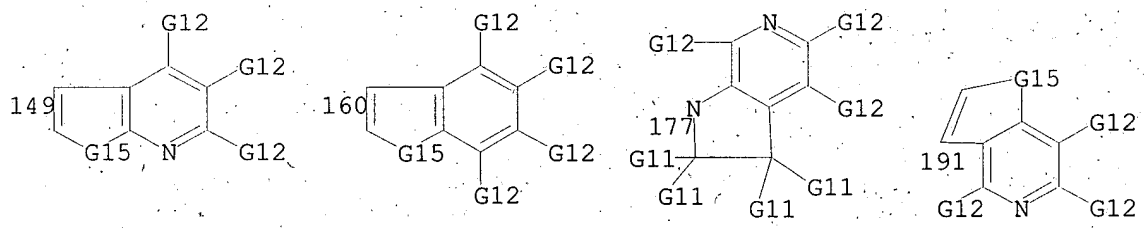


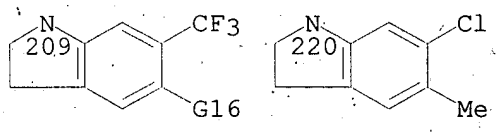


G10 = 62 / 71 / 80 / 89 / 177 / 124 / 127 / 138 / 149 /
160 / 191 / (SC 209 / 220)



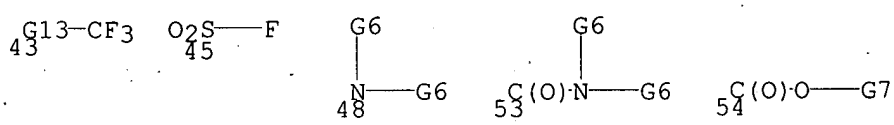




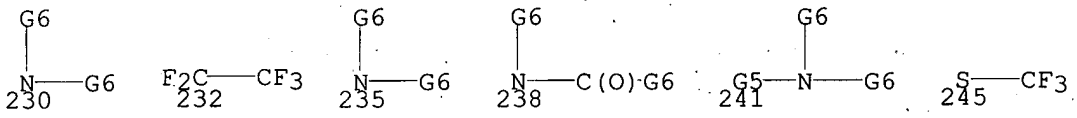


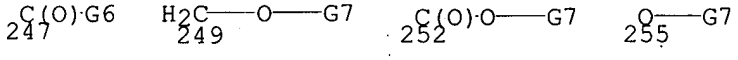
G11 = H / alkyl<(1-6)>
G12 = H / alkyl<(1-6)> (SO (1-) F) / alkenyl<(2-6)> /
cycloalkyl<(3-6)> / alkoxy<(1-6)> (SR cycloalkyl<(3-6)>) /
alkynyl<(2-6)> / cycloalkyloxy<(3-6)> /
alkyl<(1-6)> (SR cycloalkyl<(3-6)>) / alkylthio<(1-6)> /
cycloalkylthio<(3-6)> / alkylthio<(1-6)>

(SR cycloalkyl<(3-6)>) / alkoxy<(1-6)> / OH / X / NO2 / 43 / 45 / CHO / alkylcarbonyl<(1-5)> / CN / Ph (SO) / thienyl (SO) / 48 / 53 / CO2H / 54

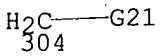


G13 = O / S / SO2
G14 = pyrazinyl (SR (-3) G12) / 2-pyridyl (SR (-4) G12) / 3-pyridyl (SR (-4) G12) / Ph (SR (-5) G12)
G15 = O / S / CH2
G16 = OMe / SMe
G17 = alkyl<(1-6)> (SO 230) / alkenyl<(2-6)> / alkynyl<(2-26)> / alkyl<(1-6)> / CN / NO2 / F / Cl / Br / I / CF3 / 232 / 235 / 238 / 241 / CHO / OCF3 / 245 / 247 / CH2OH / 249 / **CO2H** / 252 / OH / 255 / (SC Me / Et / Bu-t / OMe)

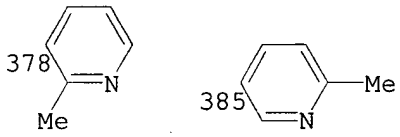




G18 = 4-pyridyl / 3-pyridyl / 304

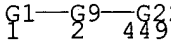


G19 = 3-pyridyl / Ph / 378 / 385



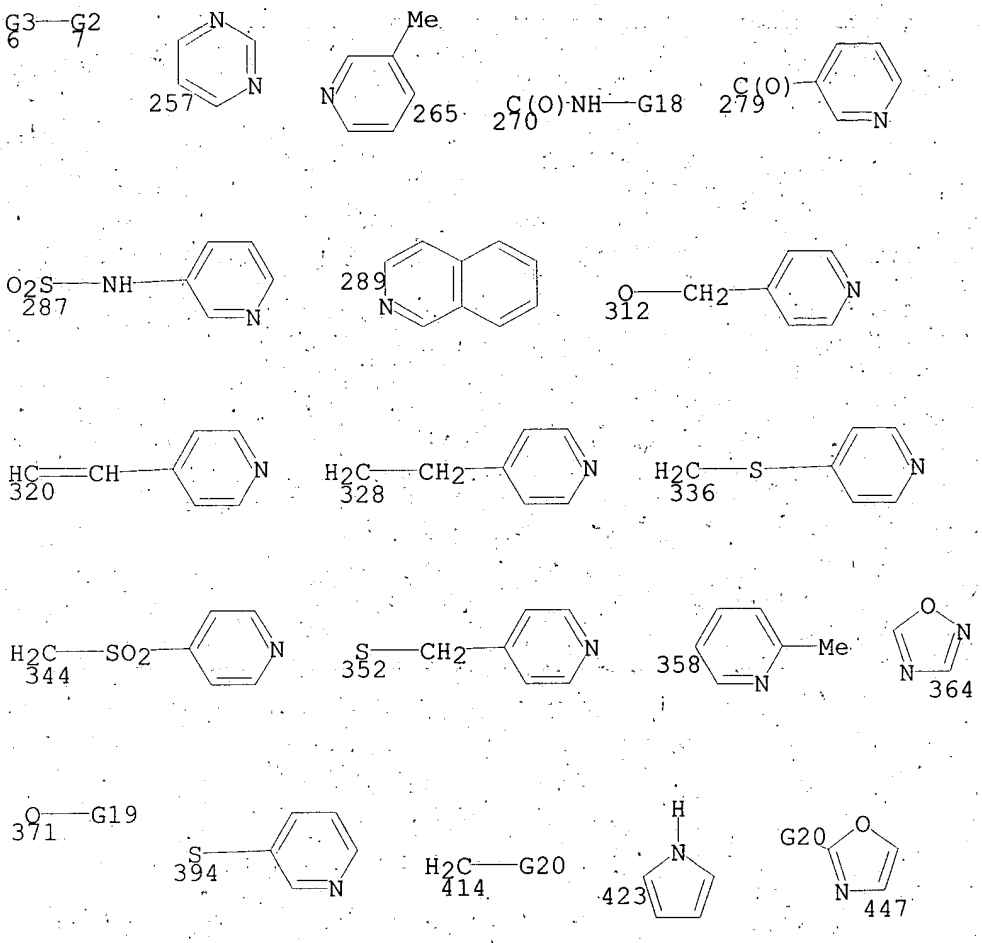
G20 = 3-pyridyl / 4-pyridyl
G21 = pyridyl
DER: and pharmaceutically acceptable salts
MPL: claim 1

MSTR 2



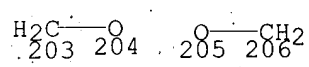
G1 = Ph (SO (-1) G4) / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO (-1) G4) / 6 / (SC pyridyl / 257 / 265 / 270 / 279 / 287 / 289 / 312 / 320 / 328 / 336 /

344 / 352 / 358 / 364 / 371 / 394 / pyrazinyl / 414 / thienyl / 423 / 2-furyl / 447)

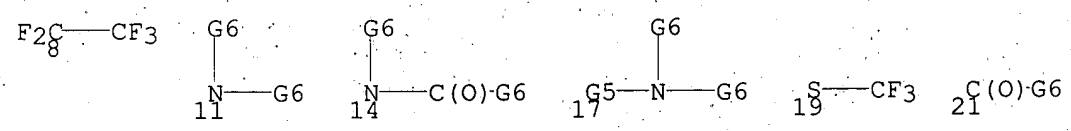


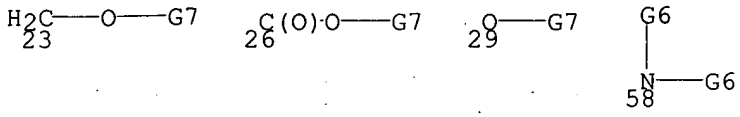
G2 = **Ph (SO (-1) G4)** / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO (-1) G4)

G3 = R<TX "chain of 1 to 5 atoms"> (SO alkyl<(1-6)>) / phenylene (SO) / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> (SO) / (SC 203-2 204-7 / **205-2 206-7** / O)

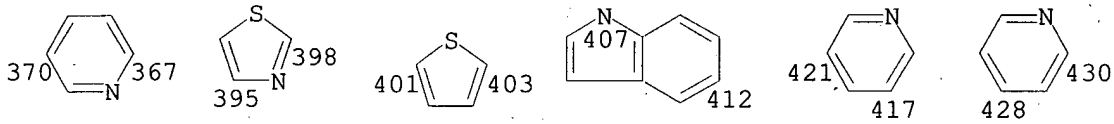


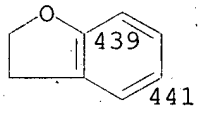
G4 = alkyl<(1-6)> (SO 58) / alkenyl<(2-6)> / alkynyl<(2-26)> / alkyl<(1-6)> / CN / NO2 / F / Cl / Br / I / CF3 / 8 / 11 / 14 / 17 / CHO / OCF3 / 19 / 21 / CH2OH / 23 / **CO2H** / 26 / OH / 29 / (SC Me)



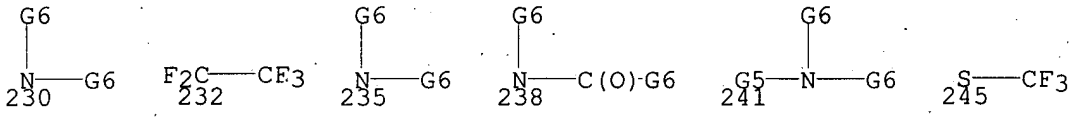


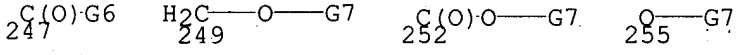
G5 = S / S(O) / SO2
G6 = H / alkyl<(1-6)> / aryl (SO) / alkyl<(1-6)> (SR aryl)
G7 = alkyl<(1-6)> / aryl (SO) / alkyl<(1-6)> (SR aryl)
G8 = H / alkyl<(1-6)>
G9 = phenylene (SO (-1) G17) / **Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO (-1) G17)** / (SC 370-449 367-1 / 395-449 398-1 / 401-449 403-1 / 412-449 407-1 / 421-449 417-1 / 428-449 430-1 / 441-449 439-1)



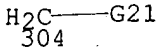


G17 = alkyl<(1-6)> (SO 230) / alkenyl<(2-6)> / alkynyl<(2-26)> / alkyl<(1-6)> / CN / NO2 / F / Cl / Br / I / CF3 / 232 / 235 / 238 / 241 / CHO / OCF3 / 245 / 247 / CH2OH / 249 / **CO2H** / 252 / OH / 255 / (SC Me / Et / Bu-t / OMe)

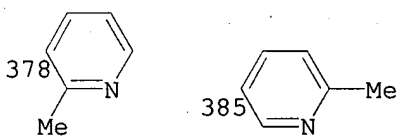




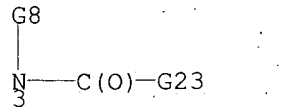
G18 = 4-pyridyl / 3-pyridyl / 304



G19 = 3-pyridyl / Ph / 378 / 385



G20 = 3-pyridyl / 4-pyridyl
G21 = pyridyl
G22 = R<TX "functional group"> / (EX NCO / 3 / NH2 / alkylamino<(1-6)> / X / NO2 / CO2H)



G23 = R<TX "leaving group"> / (EX X / Cl / Br / imidazolyl / OPh (SO) / SPh (SO))
DER: or convertible groups
DER: and pharmaceutically acceptable salts
MPL: claim 10

L3 ANSWER 44 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:195447 MARPAT
TITLE: Preparation of bicyclic aryl and heteroaryl compounds as glycoprotein IIb/IIIa antagonists
INVENTOR(S): Fisher, Matthew Joseph; Jakubowski, Joseph Anthony; Martinelli, Michael John; Morin, John Michael, Jr.; Paal, Michael; Ruhter, Gerd; Ruterbories, Kenneth James; Schotten, Theo; Stenzel, Wolfgang; Vasileff, Robert Theodore
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
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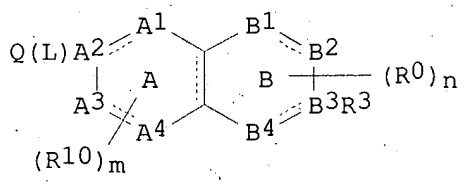
WO 9622288	A1	19960725	WO 1996-US586	19960118
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
US 5731324	A	19980324	US 1995-376191	19950119
AU 9647580	A1	19960807	AU 1996-47580	19960118
AU 706278	B2	19990610		
EP 804431	A1	19971105	EP 1996-903516	19960118
EP 804431	B1	20020724		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 11502194	T2	19990223	JP 1996-522354	19960118
BR 9607570	A	19990908	BR 1996-7570	19960118
RU 2169146	C2	20010620	RU 1997-113756	19960118
AT 220903	E	20020815	AT 1996-903516	19960118
FI 9702951	A	19970821	FI 1997-2951	19970711
NO 9703304	A	19970910	NO 1997-3304	19970717

PRIORITY APPLN. INFO.: US 1995-376191 19950119
US 1993-96220 19930722
US 1994-255821 19940708
WO 1996-US586 19960118

GI



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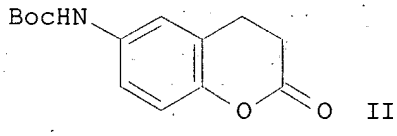

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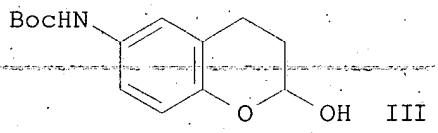

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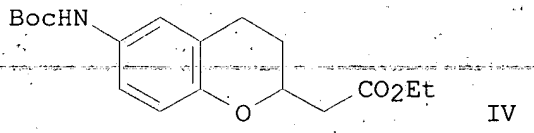

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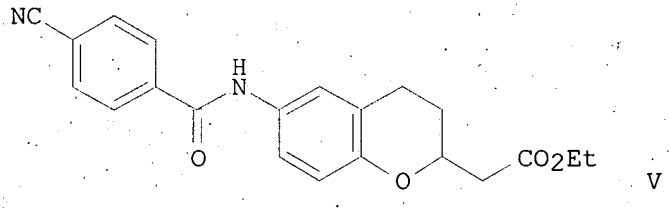


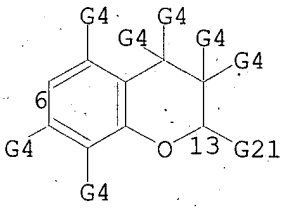
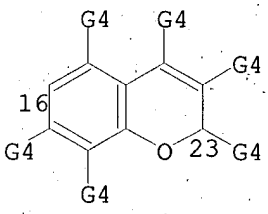
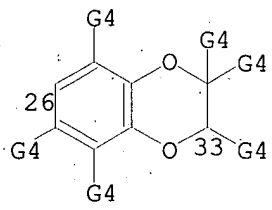
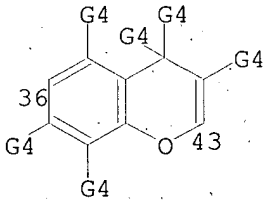
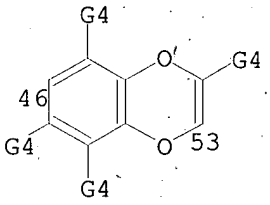
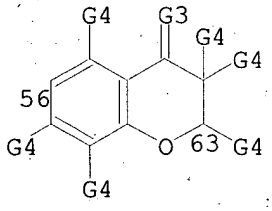
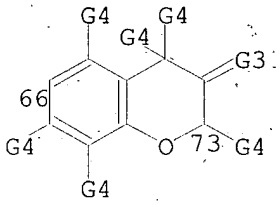
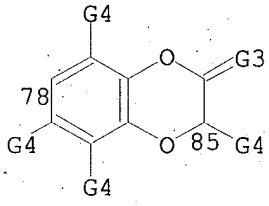
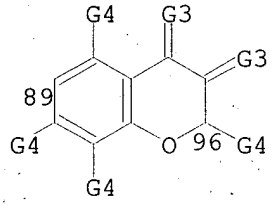
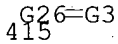
V

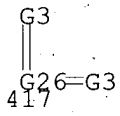
AB The title compds. [I; R0 = H, alkyl, alkenyl, etc.; R3 = acidic group contg. one or more acid radicals; R10 = H, alkyl, alkenyl, etc.; Q = basic group contg. one or more basic radicals; L = bond, (substituted) chain; n, m = 0-6; AB = benzopyran, isoquinoline, isoquinolone, tetrahydronaphthalene, dihydronaphthalene, tetralone], platelet aggregation inhibitors useful in alleviating the effects of atherosclerosis and arteriosclerosis, acute myocardial infarction, stable and unstable angina, transient ischemic attacks and strokes, arterial thrombosis, preeclampsia, embolism and restenosis, were prepd. and formulated. Thus, redn. of lactone II with DIBAL-H in CH2Cl2/PhMe followed by reaction of the intermediate III with EtOCOCH:PPh3 in PhMe, deprotection of acetate IV with TFA, reaction of unprotected acetate IV with 4-NCC6H4COCl treatment of the intermediate V with gaseous HCl in EtOH and subsequently with NH3/EtOH afforded the desired product I [AB = benzopyran; B4 = O; R1, R10 = H; R3 = CH2COOEt; QL = 4-NH:C(NH2)C6H4CONH; dotted bonds in ring A = unsatd.; dotted bonds B1B2 and B3B4 = satd.] which showed IC50 of 0.77 .mu.M against GPIIb-IIIa.

MSTR 1

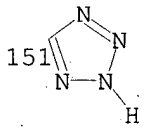
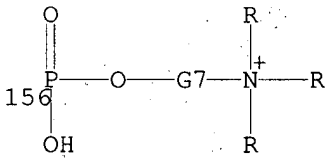
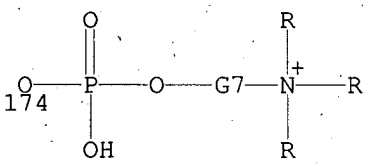
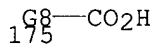
G6—G5—G23
1 2 292

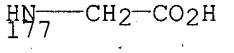
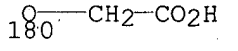
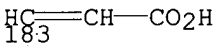
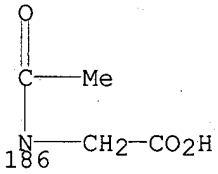
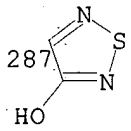
G1 = 6-2 13-4 / 16-2 23-4 / 26-2 33-4 / 36-2 43-4 /
46-2 53-4 / 56-2 63-4 / 66-2 73-4 / 78-2 85-4 / 89-2 96-4 /
(EX Cb<EC (10) C, BD (0-) D, FA (2) C, RC (2),
RS (2) E6 (0) OTHER> (SO (1-) G27) /
Hy<EC (10) A (1-6) Q (0-) N (0-) O (0-) S (0) OTHERQ (4-) C,
FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G27) / 415 /
417)



G2 = R<TX "acidic group"> / (SC SO3H / 151 / PO3H2 / OPO3H2 / 156 / 174 / 175 / CO2H / CH2CO2H / 177 / 180 / CH2CH2CO2H / 183 / 186) / (EX 287)

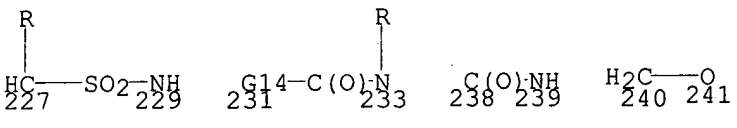






G3 = O / S

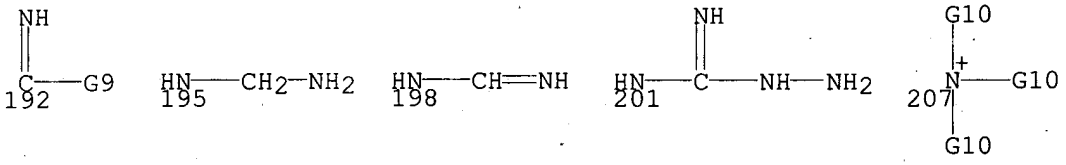
G4 = H / alkyl<(1-10)> (SO (1-) G15) / alkenyl<(2-6)> / alkynyl / cycloalkyl / aryl / alkyl<(1-10)> (SR (1-3) aryl) / OH / alkoxy<(1-10)> / alkoxy<(1-10)> (SR (1-3) aryl) /

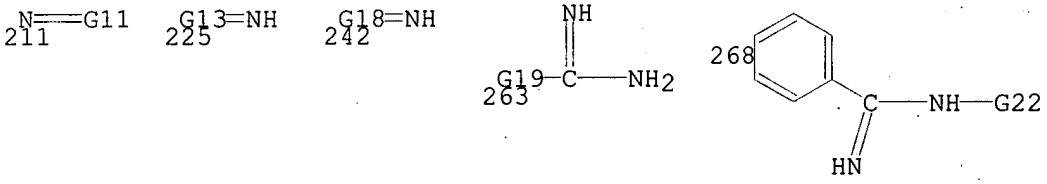
NH2 (SO) / CONH2 / **CO2H** / acyl / CN / F / Cl / Br / I / NO2 / SO3H

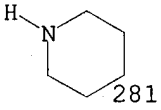
G5 = NULL / R<TX "optionally substituted linking group", EC (1-10) A (0-) Q (0-) N (0-) S (0-) O (0) OTHERQ (0-) C> / (SC 227-1 229-292 / 231-1 233-292 / ethynylene / CH=CH / CH2CH2 / 238-1 239-292 / **240-1 241-292**)



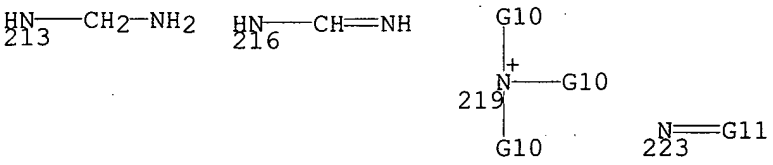
G6 = R<TX "basic group"> / (SC NH2 / 192 / 195 / 198 / NHC(NH)NH2 / 201 / alkylamino<(1-10)> / dialkylamino<(1-10)> / 207 / 211 / Hy<EC (1-4) Q (1-) N (0-) O (0-) S (0-) As (0) OTHERQ, RC (1-3), RS (0-) E5 (0-) E6 (0) OTHER> (SO G12) / CONH2 / CSNH2 / 225 / **Hy<EC (5-8) A (0-) N (0-) O (0-) S (0) OTHERQ> (SR (1-) G16)** / 242 / 263 / 268 / 281)



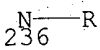




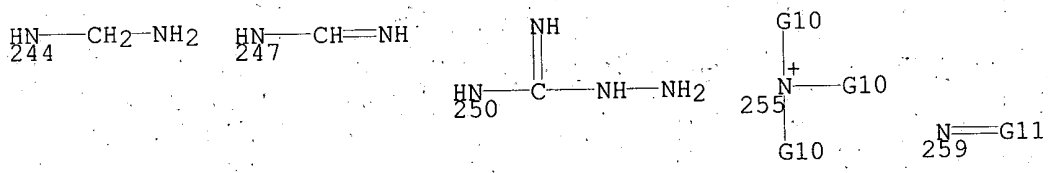
G7 = alkylene<DC (0) M3>
G8 = phenylene
G9 = NH2 / alkylamino<(1-10)> / dialkylamino<(1-10)> / arylamino
G10 = alkyl<(1-10)>
G11 = alkylidene<(1-10)>
G12 = NH2 / C(NH)NH2 / 213 / 216 / NHC(NH)NH2 / alkylamino<(1-10)> / dialkylamino<(1-10)> / 219 / 223

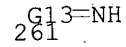


G13 = Hy<EC (1-4) Q (1-) N (0-) O (0-) S (0-) As (0) OTHERQ, RC (1-3), RS (0-) E5 (0-) E6 (0) OTHER> (SO)
G14 = 236 / O / S

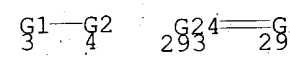


G15 = F / Cl / Br / I
G16 = (1-3) G17 / (-3) G4
G17 = R<TX "basic group"> / NH2 / C(NH)NH2 / 244 / 247 / NHC(NH)NH2 / 250 / alkylamino<(1-10)> / dialkylamino<(1-10)> / 255 / 259 / Hy<EC (1-4) Q (1-) N (0-) O (0-) S (0-) As (0) OTHERQ, RC (1-3), RS (0-) E5 (0-) E6 (0) OTHER> (SO) / 261

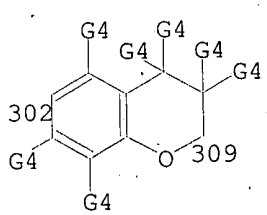


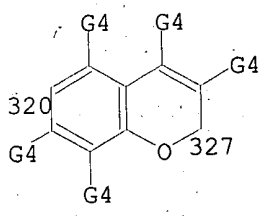


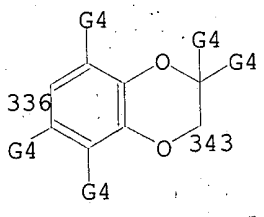
G18 = Hy<EC (5-8) A (0-) N (0-) O (0-) S (0) OTHERQ> (SO)
G19 = p-C6H4 (SO (1-) G20)
G20 = R / F / Cl
G21 = H / alkyl<(1-10)> (SO (1-) G15) / alkenyl<(2-6)> / alkynyl / cycloalkyl / aryl / alkyl<(1-10)> (SR (1-3) aryl) / OH / alkoxy<(1-10)> / alkoxy<(1-10)> (SR (1-3) aryl) / NH2 (SO) / CONH2 / CO2H / acyl / CN / F / Cl / Br / I / NO2 / SO3H / (SC Me)
G22 = Me / Et / Pr-n / CH2Ph
G23 = 3 / 293

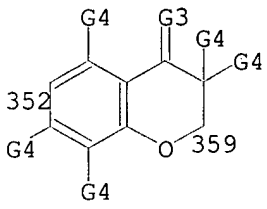


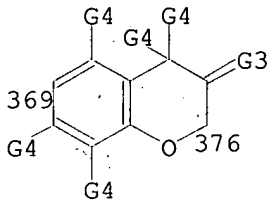
G24 = 302-2 309-294 / 320-2 327-294 / 336-2 343-294 / 352-2 359-294 / 369-2 376-294 / 386-2 393-294 / 401-2 408-294 / (EX Cb<EC (10) C, BD (0-) D, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G27) / Hy<EC (10) A (1-6) Q (0-) N (0-) O (0-) S (0) OTHERQ (4-) C, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G27) / 420 / 422)

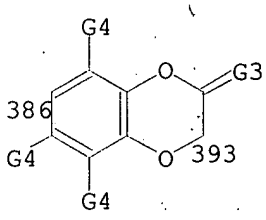


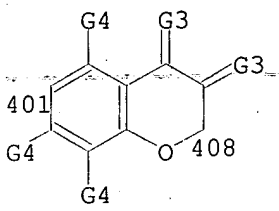




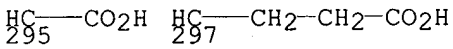








G25 = R<TX "acidic group"> / (SC 295 / 297)



G26 = Cb<EC (10) C, BD (0-) D, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G27) / Hy<EC (10) A (1-6) Q (0-) N (0-) O (0-) S (0) OTHERQ (4-) C, FA (2) C, RC (2), RS (2) E6 (0) OTHER> (SO (1-) G27)
G27 = alkyl<(1-10)> (SO (1-) G15) / alkenyl<(2-6)> / alkynyl / cycloalkyl / aryl / alkyl<(1-10)> (SR (1-3) aryl) / OH / alkoxy<(1-10)> / alkoxy<(1-10)> (SR (1-3) aryl) / NH2 (SO) / CONH2 / **CO2H** / acyl / CN / F / Cl / Br / I / NO2 / SO3H
DER: or pharmaceutically acceptable salts, solvates or prodrugs
MPL: claim 1
NTE: also incorporates broader disclosure
NTE: substitution is restricted

L3 ANSWER 45 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 124:325016 MARPAT
TITLE: Skin-lightening cosmetics containing benzoin acid derivatives as melanin formation inhibitors
INVENTOR(S): Suzuki, Yasuto; Oohashi, Yukihiro; Nishizawa, Yoshinori; Kimura, Mitsutoshi; Morizaki, Naoko; Yada, Yukihiro; Imokawa, Genji
PATENT ASSIGNEE(S): Kao Corp, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 29 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08048621	A2	19960220	JP 1995-126842	19950525
PRIORITY APPLN. INFO.:			JP 1994-120370	19940601

AB Skin-lightening cosmetics contain benzoic acid derivs. such as Me 4-benzyloxy-2-hydroxybenzoate and 4-benzyloxy-2-hydroxybenzoic acid as

melanin formation inhibitors. 4-Benzyloxy-2-hydroxybenzoic acid was prepd. by the hydrolysis of Me 4-benzyloxy-2-hydroxybenzoate. A skin-lightening lotion contained 4-benzyloxy-2-hydroxybenzoic acid 0.5, ethoxylated hardened castor oil 1.5, glycerin 4.0, ethanol 10.0, sodium pyrrolidonecarboxylate 2.0, perfumes, and purified water to 100 wt.%. The prepns. were safe and effective.

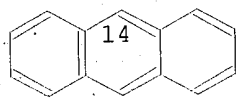
MSTR 1

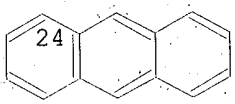
G4—C(O)-G2—G1

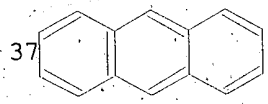
G1 = H / OH / CO2H / loweralkoxy / loweralkoxycarbonyl / (EX OMe)
G2 = **o-C6H4 (SR (1) G3)**
G3 = aralkyloxy (SO G7) / aryloxy (SO G8) / alkoxy (SR heteroaryl (SO G8)) / heteroaryloxy / **(SC 5)**

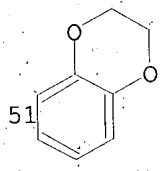
O—G5—G6
5

G4 = **OH** / loweralkoxy / (EX OMe)
G5 = **(1-6) CH2**
G6 = naphthyl / 14 / 24 / 37 / **Ph (SR (1) CO2H)** / Ph (SR (1-2) OH) / pyridyl / 51









G7 = R / (EX Me / OH / OMe)
G8 = R / (EX OH / Bu-t / OMe)
DER: or salts
MPL: claim 1

L3 ANSWER 46 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 124:261073 MARPAT
TITLE: Bis mono- and bicyclic aryl and heteroaryl compounds which inhibit EGF and/or PDGF receptor tyrosine kinase
INVENTOR(S): Spada, Alfred P.; Myers, Michael R.; Maguire, Martin P.; Persons, Paul E.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: U.S., 33 pp. Cont.-in-part of U.S. Ser. No. 988,515, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5480883	A	19960102	US 1993-166199	19931210
US 5710158	A	19980120	US 1994-229886	19940419
WO 9515758	A1	19950615	WO 1994-US14180	19941208

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,

GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW,
NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN,
TD, TG

AU 9513050	A1	19950627	AU 1995-13050	19941208
EP 871448	A1	19981021	EP 1995-904308	19941208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
US 5656643	A	19970812	US 1995-385258	19950208
US 5795889	A	19980818	US 1995-386271	19950209
US 5646153	A	19970708	US 1995-439027	19950511
US 5721237	A	19980224	US 1995-469147	19950606
US 5714493	A	19980203	US 1996-652444	19960604
US 6057320	A	20000502	US 1997-881991	19970625
US 36256	E	19990720	US 1997-988005	19971210
AU 739382	B2	20011011	AU 1999-65543	19991230
AU 9965543	A1	20000323		
US 37650	E	20020409	US 2000-496399	20000202
PRIORITY APPLN. INFO.:			US 1991-698420	19910510
			US 1992-988515	19921210
			WO 1992-US3736	19920506
			US 1993-146072	19931108
			US 1993-166199	19931210
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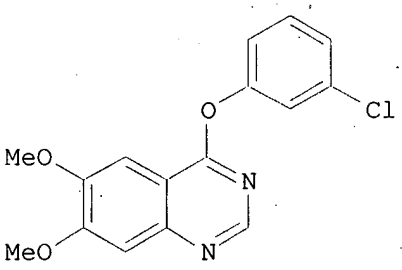
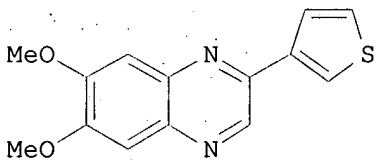
			WO 1994-US14180	19941208
			US 1995-439027	19950511
			US 1996-652444	19960604

GI



II



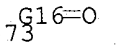
III

AB The invention relates to bis mono- and/or bicyclic aryl and/or heteroaryl compds. Ar1XAr2 [I; Ar1, Ar2 = (un)substituted mono- or bicyclic rings with 0-3 substituents; X = (CHR1)0-4 or (CHR1)mZ(CHR1)n; Z = O, NR2; S, SO, SO2; m, n = 0-3; R1, R2 = H, alkyl] exhibiting protein tyrosine kinase inhibition activity. I inhibit abnormal cell proliferation in proliferative disorders by selectively inhibiting EGF and/or PDGF receptor. Approx. 300 compds. I are listed with characterizing data, and biol. data for selected compds. are given. For example, m-ClC6H4OH was treated with NaH in THF, followed by 4-chloro-6,7-dimethoxyquinazoline, to give title compd. II. The claimed quinoxaline deriv. III inhibited PDGF-R cell-free autophosphorylation with an IC50 of 0.02-0.05 .mu.M.

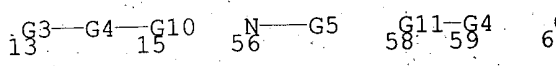
MSTR 2A

G1 = Cb<AR (0)> (SO (1-3) G9) /
aryl<EC (6-12) C, RC (1-2)> (SO (1-3) G9) /

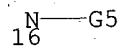
Hy<EC (5-12) A (-4) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / 73 / (EX Ph (SO) / quinolinyl / thienyl (SO))



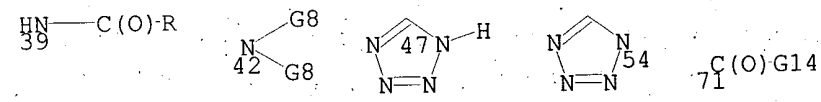
G2 = alkylene / CH2 / CH2CH2 / CH2CH2CH2 / 13-9 15-12 / O / NH / S / S(O) / SO2 / 56 / 58-9 59-12 / 60-9 61-12



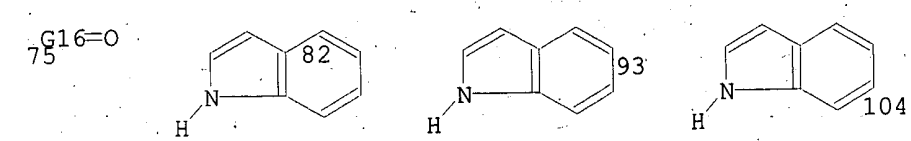
G3 = alkylene / CH2 / CH2CH2 / CH2CH2CH2
G4 = **O** / NH / S / S(O) / SO2 / 16

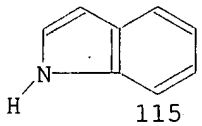


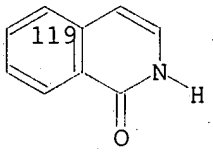
G5 = alkyl
G7 = F / Cl / Br / I
G8 = cycloalkyl
G9 = alkyl / alkenyl / aralkyl / alkenyl (SR (1-) aryl) / OH / alkyl (SR OH) / alkoxy / alkyl (SR alkoxy) / aralkyloxy / acyloxy / F / Cl / Br / I / alkyl (SR (1-) G7) / NO2 / NH2 / alkylamino / dialkylamino / acylamino / **CO2H** / alkyl (SR CO2H) / alkoxycarbonyl / aralkyloxycarbonyl / alkyl (SR alkoxycarbonyl) / alkenyl (SR alkoxycarbonyl) / alkoxy (SR NH2) / 39 / alkylamino / dialkylamino / 42 / Ph (SO (1-) G7) / Hy<EC (1) S (0) OTHERQ (4) C, RC (1), BD (2) D, RS (1) E5 (0) OTHER> (SO (1-) G7) / Hy<EC (1) N (5) C (0) OTHERQ, RC (1), AR (1-), BD (ALL) N, RS (1) E6 (0) OTHER> / 47 / 54 / 71

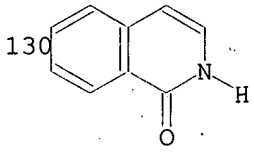


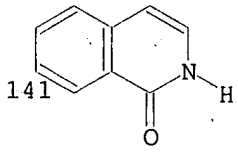
G10 = alkylene / CH2 / CH2CH2 / CH2CH2CH2
G11 = alkylene / CH2 / CH2CH2 / CH2CH2CH2
G12 = alkylene / **CH2** / CH2CH2 / CH2CH2CH2
G14 = Cb<EC (6) C, AR (1-), BD (ALL) N, RC (1), RS (1) E6>
G15 = Cb<AR (0)> (SO (1-3) G9) / **aryl<EC (6-12) C, RC (1-2)> (SO (1-3) G9)** / Hy<EC (5-12) A (-4) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO (1-3) G9) / 75 / (EX pyridyl / Ph / naphthyl / 82 / 93 / 104 / 115 / pyrimidinyl / 119 / 130 / 141 / 158 / 167 / 178 / 189 / 206 / 215 / 224 / 233 / 248 / 261 / 272 / 281 / 293 / 301 / 312 / 323 / 332 / 343 / 351 / 362 / 373 / 382 / 393 / 401 / 409 / 419 / 429 / 439)

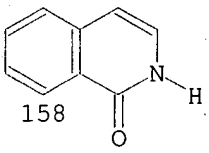


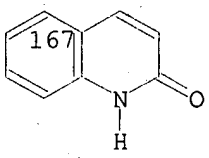


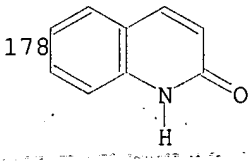


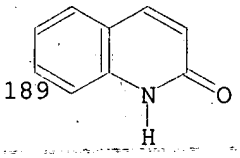


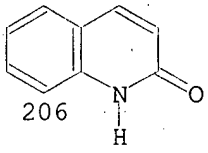


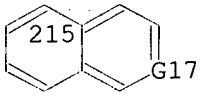


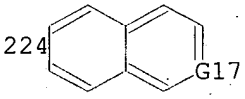


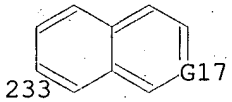


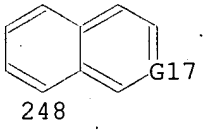


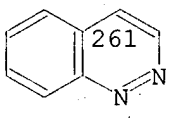


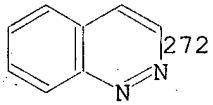


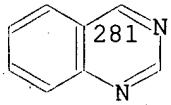


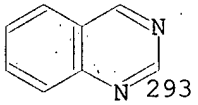


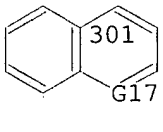


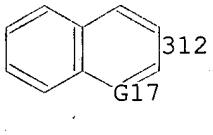


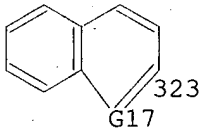


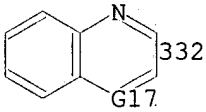


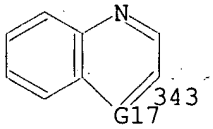


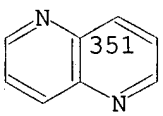


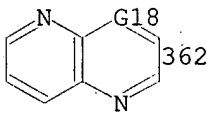


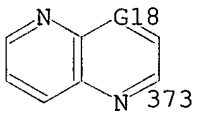


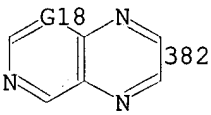


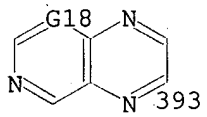


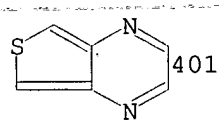


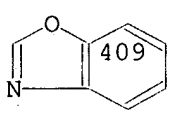


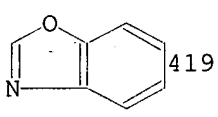


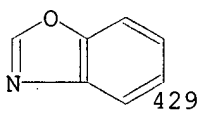


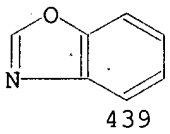






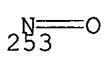






G16 = Cb<AR (0)> (SO) / Cb<EC (6-12) C, AR (1-), RC (1-2)> (SO) / Hy<EC (5-12) A (-4) Q (0-) O (0-) S (0-) N (0) OTHERQ, RC (1-2)> (SO)

G17 = N / 253

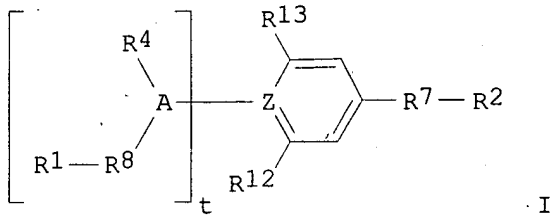


G18 = N / CH
DER: and pharmaceutically acceptable salts
MPL: disclosure

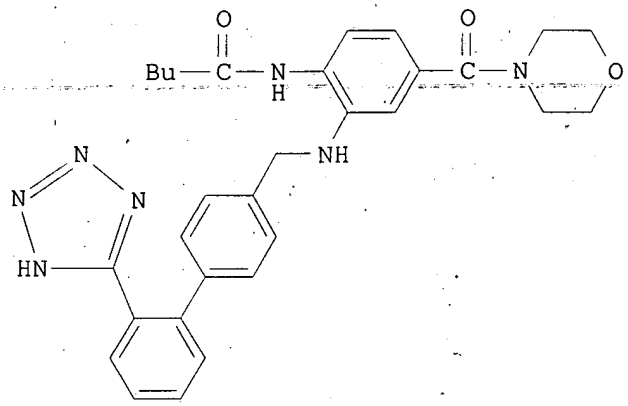
L3 ANSWER 47 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 124:202284 MARPAT
TITLE: Benzene derivatives [(tetrazolylbiphenylyl)-substituted benzoic acid morpholides and analogs] for treatment of kidney disease, and pharmaceutical compositions containing them
INVENTOR(S): Yanaka, Mikiro; Nishijima, Fuyuhiko; Enari, Hiroyuki; Dewa, Toshikazu; Yamazaki, Toru; Ise, Michihito
PATENT ASSIGNEE(S): Kureha Chemical Industry Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 685470	A2	19951206	EP 1995-108406	19950601
EP 685470	A3	19960207		
EP 685470	B1	20020911		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL				
CA 2150610	AA	19951202	CA 1995-2150610	19950531
AU 9520428	A1	19960104	AU 1995-20428	19950601
AU 675035	B2	19970116		
JP 08048651	A2	19960220	JP 1995-158659	19950601
JP 2796265	B2	19980910		
US 5696118	A	19971209	US 1995-457147	19950601
AT 223908	E	20020915	AT 1995-108406	19950601
US 5731310	A	19980324	US 1996-702116	19960823
US 5739131	A	19980414	US 1997-841621	19970430
PRIORITY APPLN. INFO.:			JP 1994-142276	19940601
			US 1995-457147	19950601

GI



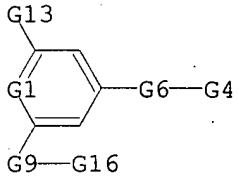
I



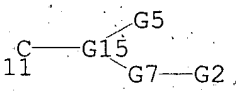
II

AB Title compds. I [R1 = H, alkyl, haloalkyl, NH2, NHR21; R2 = OH, OR22, 3- to 7-membered satd. cycloaliph. amino optionally interrupted by N, O, or S atom(s), NHR23, N(R24)2, NH2; R4 = H, alkyl, or COR25; R7 = CO, SO2; R8 = CO, bond; R12 = R11-R5; R11 = N(R5), NH, O, N(R26), N(COR27), N(CONH2), N(CONHR28); R13 = H, alkyl, haloalkyl, NHCO(CH2)mPh, NHCOR29, NHCOCHPh2, NH2, NHR30, (CH2)nPh; Z = C, CH, N; A = CH, N; R5 = H, CH2C6H4COOH, CH2C6H4COOR31, CH2C6H4OH, CH2C6H4OR32, CH2C6H4NH2, CH2C6H4N(R33)2, CH2C6H4-azole, CH2C6H4NHR34, CH2C6H4C6H4R14; R14 = azole, COOH; R21-R34 = alkyl or haloaklyl; m = 0-6; n = 0-6; t = 0 or 1, with the proviso that when Z = N, R5 = H, CH2C6H4COOH, CH2C6H4NHR34], and salts thereof are disclosed, as well as pharmaceutical compns. comprising I or salts and a pharmaceutically acceptable carrier. I are effective for treating renal dysfunction without affecting blood pressure. For example, 3-nitro-4-valeramidobenzoic acid underwent conversion to the morpholide using DCC and HOBt, redn. of the nitro group by hydrazine and Pd/C, alkylation of the resulting amino group with N-(triphenylmethyl)-5-[4'-(bromomethyl)biphenyl-2-yl]tetrazole, and finally deprotection with concd. HCl in MeOH-THF, to give title compd. II. In a rat kidney disease model, II at 20 mg/kg/day increased av. survival time from 5.0 wk (control) to 7.3 wk, whereas the known compd. DuP753 increased survival time to 6.9 wk. I did not show angiotensin II receptor antagonism or hypotensive activity, and were nonlethal at 500 mg/kg orally in mice.

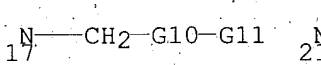
MSTR 1



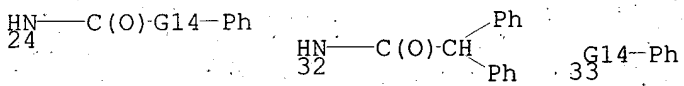
G1 = N / 11 / **CH**



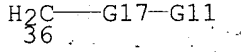
G2 = H / alkyl<(1-6)> (SO (1-) G3) / NH2 /
alkylamino<(1-6)> (SO (1-) G3)
G3 = F / Cl / Br / I
G4 = **OH** / alkoxy<(1-6)> (SO (1-) G3) /
Hy<EC (1-2) Q (1-2) N (-1) O (-1) S (0) OTHERQ, BD (ALL) SE,
AN (1) N, RC (1), RS (1) M4 (1) X7> /
alkylamino<(1-6)> (SO (1-) G3) /
dialkylamino<(1-6)> (SO (1-) G3) / NH2 / (EX azetidino /
pyrrolidino / piperidino / morpholino / thiomorpholino /
piperazino)
G5 = H / alkyl<(1-6)> / alkylcarbonyl<(1-6)> (SO (1-) G3)
G6 = **C(O)** / SO2
G7 = NULL / C(O)
G9 = NH / 17 / **O** / 21



G10 = phenylene
G11 = **CO2H** / alkoxycarbonyl<(1-6)> (SO (1-) G3) / OH /
alkoxy<(1-6)> (SO (1-) G3) / NH2 /
dialkylamino<(1-6)> (SO (1-) G3) /
Hy<EC (2-4) Q (1-3) C (0-) O (0-) N (0-) S (0) OTHERQ,
RC (1), RS (1) E5> / alkylamino<(1-6)> (SO (1-) G3) /
(SC tetrazolyl)
G12 = alkyl<(1-6)> (SO (1-) G3) /
alkylcarbonyl<(1-6)> (SO (1-) G3) / CONH2 /
alkylaminocarbonyl<(1-6)> (SO (1-) G3)
G13 = H / alkyl<(1-6)> (SO (1-) G3) / 24 /
alkylcarbonylamino<(1-6)> (SO (1-) G3) / 32 / NH2 /
alkylamino<(1-6)> (SO (1-) G3) / 33



G14 = (0-6) CH2
G15 = CH / N
G16 = H / **36**



G17 = **phenylene**
DER: or salts
MPL: claim 1

L3 ANSWER 48 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 123:198609 MARPAT
TITLE: Synthesis of diarylmethanols by rearrangement of aryl arylmethyl ethers in presence of alkali metal amide or alkali metal alkoxide
INVENTOR(S): Fang, Francis G.
PATENT ASSIGNEE(S): Glaxo Inc., USA

SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5426196	A	19950620	US 1993-173289	19931222
WO 9517408	A1	19950629	WO 1994-US14327	19941220
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9514348	A1	19950710	AU 1995-14348	19941220
PRIORITY APPLN. INFO.:			US 1993-173289	19931222
			WO 1994-US14327	19941220

OTHER SOURCE(S): CASREACT 123:198609
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

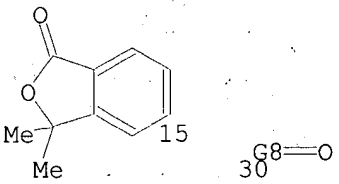
AB A method is claimed for synthesizing a diarylmethane I wherein: Y is oxygen or sulfur; A, B, C, D, and E are carbon or 1, 2 or 3 of A, B, C, D, and E are independently nitrogen, and the others are carbon; and wherein R1 through R10 are selected independently from the group consisting of: hydrogen, hydroxy, alkyl, C3-C8 cycloalkyl, C3-C8 cycloalkyl alkyl, alkenyl, hydroxy alkyl, alkoxy alkyl, perhalo-alkyl, amino, nitro, nitrile, halo oxo, carboxyl, sulfonyl, acyl, formyl, carbamoyl, trifluoromethyl, aminomethyl, azido, amido, hydrazino, aryl, aryloxy, heteroaryl, or aryl or heteroaryl (mono, di, or tri substituted) and the pharmaceutically acceptable salts and solvates thereof; and wherein; adjacent substituents on either the "a" ring or "b" ring may be joined together to form a fused ancillary 5 or 6 atom carbocyclic or heterocyclic ring structure wherein substituents on the ancillary ring structure may each independently be as represented for R1 through R10 above and the pharmaceutically acceptable salts and solvates thereof; comprising reacting: (i) an ether II wherein R1 through R10 are as described above; and (ii) alkali metal amide base or alkali metal alkoxy base. Thus, e.g, rearrangement of 5-(2,6-difluoro-4-nitrophenoxymethyl)-3,3-dimethyl-3H-isobenzofuran-1-one (III) in presence of sodium hexamethyldisilazide in THF afforded 5-[(2,6-difluoro-4-nitrophenyl)hydroxymethyl]-3,3-dimethyl-3H-isobenzofuran-1-one (IV) in 76.3% yield.

MSTR 1

G2—G5—G2
1 3

G1 = OH / SH
G2 = **Ph (SO (1-) G3)** / pyridyl / pyridazinyl / pyrimidinyl / pyrazinyl / triazinyl / Hy<EC (1-3) Q (1-3) N (0) OTHERQ (3-5) C, AN (1-) C, AR (1-), BD (6) N, RC (1), RS (1) E6> (SO (1-) G3) / 30 /

Cy<EC (0-) Q (-3) N, AN (1-) C, AR (1-), BD (6-) N, RC (2),
RS (0-) E5 (1-) E6 (0) OTHER> (SO (1-) G3) / (EX 15)



G3 = OH / alkyl<(1-15)> (SO cycloalkyl<(3-8)>) /
cycloalkyl<(3-8)> / alkenyl<(2-15)> / alkyl<(1-15)> (SR OH) /
alkyl<(1-15)> (SR alkoxy<(1-15)>) /
alkyl<EC (1-15) C (0) H> (SR (3-) G4) / NH2 / NO2 / CN / F /
Cl / Br / I / **CO2H** / 26 / acyl / CONH2 / CF3 / CH2NH2 / N3 /
20 / NHNH2 / aryl (SO (1-3) G7) / aryloxy /
heteroaryl (SO (1-3) G7)

HN──C(O)-R O2S──R
20 26

G4 = F / Cl / Br / I
G5 = 4 / **6-1 7-3**

HC──G1 G6──CH2
4 6 7

G6 = **O** / S
G7 = OH / alkyl<(1-15)> (SO cycloalkyl<(3-8)>) /
cycloalkyl<(3-8)> / alkenyl<(2-15)> / alkyl<(1-15)> (SR OH) /
alkyl<(1-15)> (SR alkoxy<(1-15)>) /
alkyl<EC (1-15) C (0) H> (SR (3-) G4) / NH2 / NO2 / CN / F /
Cl / Br / I / CO2H / 28 / acyl / CONH2 / CF3 / CH2NH2 / N3 /
23 / NHNH2 / aryl / aryloxy / heteroaryl

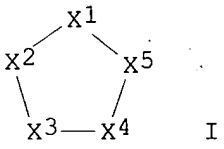
HN──C(O)-R O2S──R
23 28

G8 = Cy<EC (0-3) Q (0-3) N (0) OTHERQ (3-6) C,
AN (2-) C, AR (0), BD (2) D, RC (1), RS (1) E6> (SO (1-) G3)
DER: and pharmaceutically acceptable salts and solvates
MPL: claim 1

L3 ANSWER 49 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 122:214087 MARPAT
TITLE: 5-Member heterocyclic antithrombotics and blood platelet aggregation inhibitors
INVENTOR(S): Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard; Pieper, Helmut; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE: Ger. Offen., 35 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4302051	A1	19940728	DE 1993-4302051	19930126
CA 2114178	AA	19940727	CA 1994-2114178	19940125
NO 9400261	A	19940727	NO 1994-261	19940125
JP 07002851	A2	19950106	JP 1994-6295	19940125
CN 1097753	A	19950125	CN 1994-100575	19940125
ZA 9400495	A	19950725	ZA 1994-495	19940125
FI 9400378	A	19940727	FI 1994-378	19940126
EP 608858	A1	19940803	EP 1994-101125	19940126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AU 9453984	A1	19940804	AU 1994-53984	19940127
PRIORITY APPLN. INFO.:			DE 1993-4302051	19930126

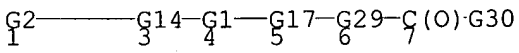
GI



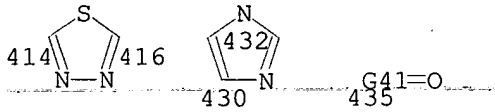
I

AB The title compds. [I; X1-X5 = C- or heteroatom-contg. (heteroatom) substituents], useful as antithrombotics and blood platelet aggregation inhibitors (no data), are prepd. and I-contg. formulations presented. Thus, 1-[6-(4-amidinophenyl)-3-pyridazinyl]-4-[2-(n-butanesulfonylamino)-2-carboxyethyl]imidazole hydrochloride was prepd. and demonstrated an ED50 of 40 nM in a collagen-induced blood platelet aggregation assay.

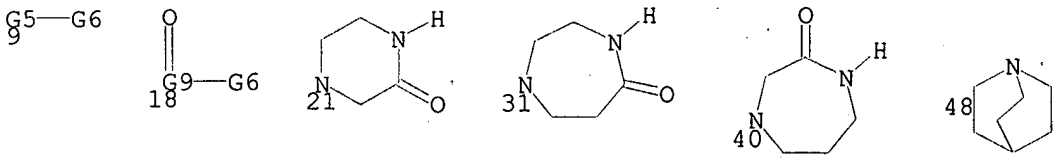
MSTR 1B

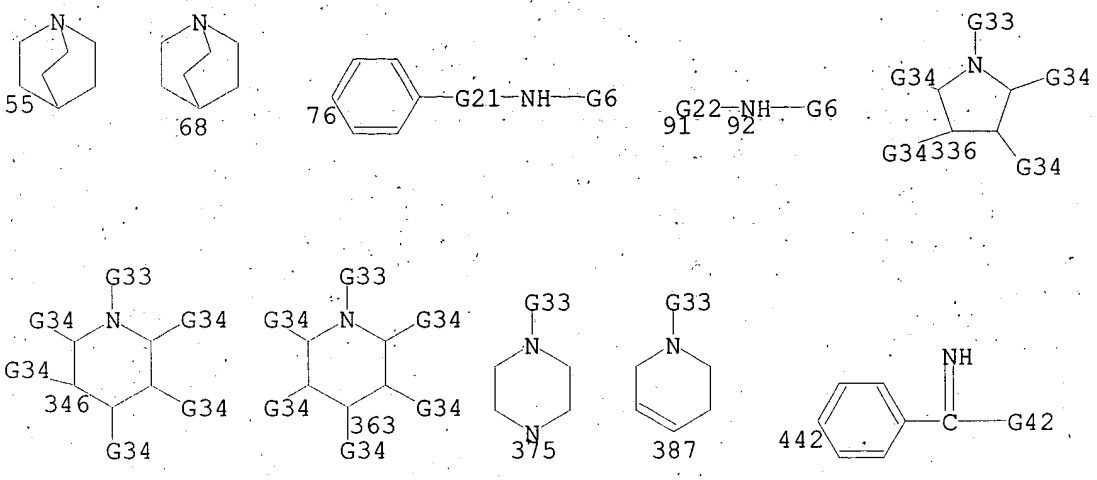


G1 = **Hy<EC (1-) Q (0-) N (-2) S (-1) O (0) OTHERQ, RC (1), RS (1) E5> (SO (1-3) G32)** / Hy<EC (1-) Q (0-) N (-2) S (-1) O (0) OTHERQ, AR (1-), BD (6) N, RC (2), RS (1) E5 (1) E6 (0) OTHER> (SO) / 435 / (SC 414-3 416-5 / 432-3 430-5)



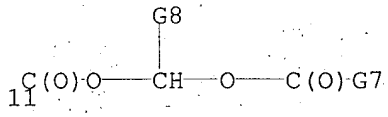
G2 = cycloalkyl<(5-7)> (SO (1-) G3) / 9 / 18 / 21 / 31 / 40 / pyridyl / 48 / 55 / 68 / 76 / 91 / 442 / 446 / (SC 336 / 346 / 363 / 375 / 387)



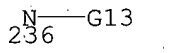


p-C_6H_4CN
446

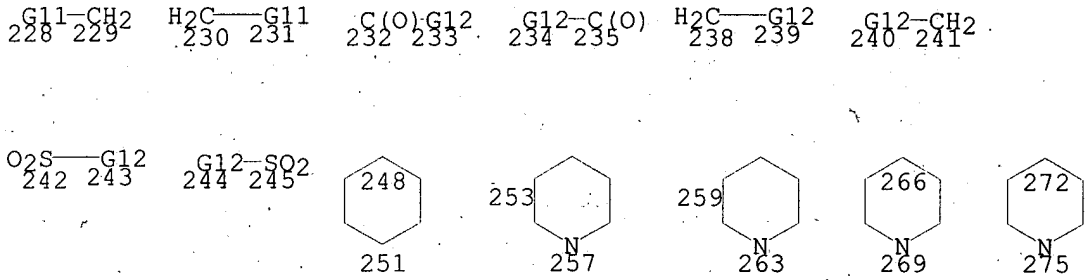
G3 = (-4) alkyl<(1-3)> / (-1) G4
G4 = OH / alkoxy<(1-3)> (SO Ph) / CN / CONH2 / **CO2H** / alkoxycarbonyl<(1-3)> (SO Ph)
G5 = **Hy<EC (4-6) C (1-2) Q (1-2) N (0) OTHERQ, AN (1-) C (1-) N, AR (0), BD (-1) DE (0) T> (SO (1-) G3)**
G6 = H / alkyl<(1-3)> / alkoxycarbonyl<(1-5)> / alkoxycarbonyl<(1-3)> (SR Ph) / alkenyloxycarbonyl<(3-5)> / cycloalkyloxycarbonyl<(5-7)> / 11

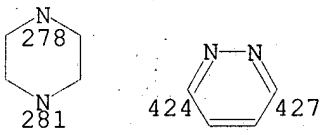


G7 = alkyl<(1-5)> / cycloalkyl<(5-7)> / alkyl<(1-3)> (SR (1-) Ph) / alkoxy<(1-5)> / cycloalkyloxy<(5-7)> / Ph
G8 = H / alkyl<(1-4)> / cycloalkyl<(5-7)> / Ph
G9 = Hy<EC (4-6) C (2) Q (2) N, AN (1-) C (2) N, AR (0), BD (-1) DE (0) T> (SO (1-) G3)
G11 = **O** / S
G12 = NH / 236

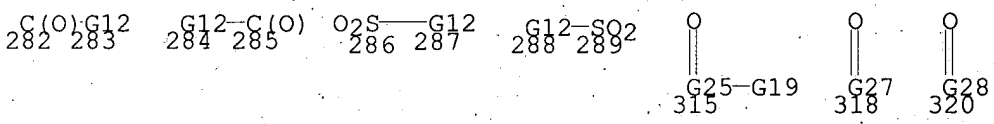


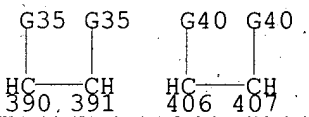
G13 = alkyl<(1-3)> (SO (1-) Ph)
G14 = phenylene / Cb<EC (6) C, AN (2-) C, AR (1-), BD (ALL) N, RC (1), RS (1) E6> (SO (1-2) G15) / Hy<EC (1-2) Q (1-2) N (0) OTHERQ, AN (2-) C (0) N, AR (1-), BD (ALL) N, RC (1), RS (1) E6> (SO G16) / 248-1 251-4 / 257-1 253-4 / 263-4 259-1 / 269-1 266-4 / 272-1 275-4 / 278-1 281-4 / alkylene / 228-1 229-4 / **230-1 231-4** / 232-1 233-4 / 234-1 235-4 / 238-1 239-4 / 240-1 241-4 / 242-1 243-4 / 244-1 245-4 / (SC 424-1 427-4 / CH2CH2)



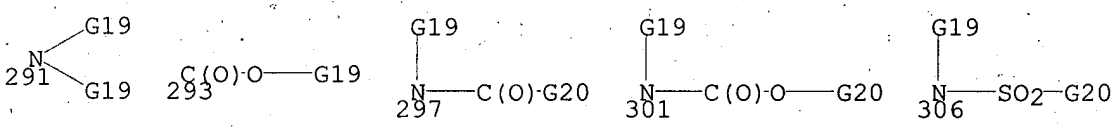


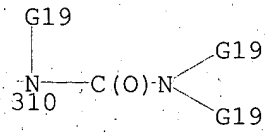
G15 = F / Cl / Br / alkyl<(1-3)> / CF3 / OH /
alkoxy<(1-3)> / alkylthio<(1-3)> / alkylsulfinyl<(1-3)> /
alkylsulfonyl<(1-3)> / (SC Me)
G16 = Cl / alkyl<(1-3)> / alkoxy<(1-3)>
G17 = 282-4 283-6 / 284-4 285-6 / 286-4 287-6 /
288-4 289-6 / Ak<EC (-8) C, BD (0-) D (0) T> (SO (1-) G18) /
phenylene / Cb<EC (6) C, AN (2-) C, AR (1-), BD (ALL) N,
RC (1), RS (1) E6> (SO (1-2) G23) /
Hy<EC (1-3) Q (1-3) N (0) OTHERQ, AN (2-) C (0) N, AR (1-),
BD (ALL) N, RC (1), RS (1) E6> (SO G24) / 315 /
cycloalkylene<(4-7)> (SO G20) /
Hy<EC (1-2) Q (1-2) N (0) OTHERQ, AR (0), BD (ALL) SE,
RC (1), RS (1) M4 (1) X7> (SO G20) / 318 / 320 /
(SC cyclohexylene / 390-4 391-6 / 406-4 407-6)





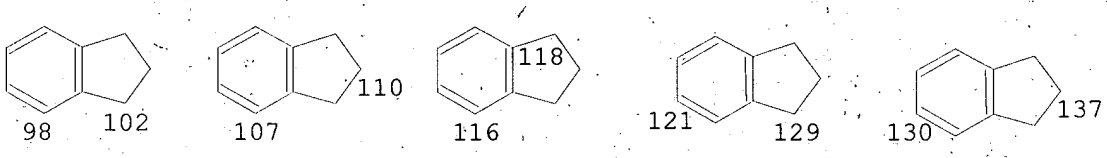
G18 = OH / alkoxy<(1-3)> / alkylthio<(1-3)> / 291 / 293 /
297 / 301 / 306 / 310

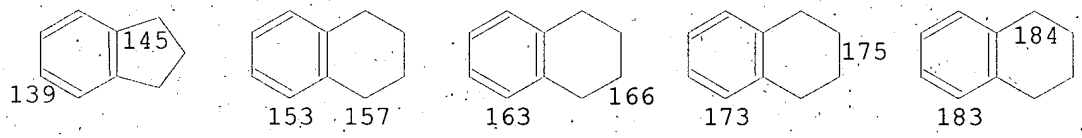


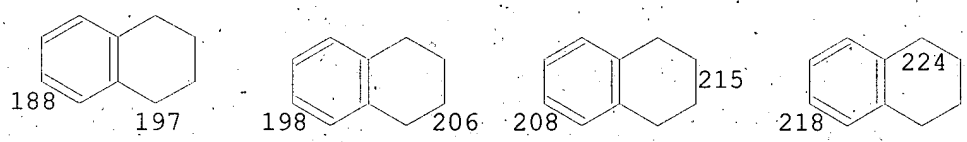


G19 = H / alkyl<(1-3)> (SO (1-) Ph)
G20 = alkyl<(1-5)> / alkyl<(1-3)> (SR (1-) Ph) / Ph
G21 = CH2 / 83

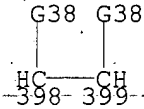
G22 = 102-92 98-3 / 110-92 107-3 / 118-92 116-3 /
129-92 121-3 / 137-92 130-3 / 145-92 139-3 / 157-92 153-3 /
166-92 163-3 / 175-92 173-3 / 184-92 183-3 / 197-92 188-3 /
206-92 198-3 / 215-92 208-3 / 224-92 218-3



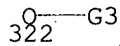




G23 = F / Cl / Br / alkyl<(1-3)> / CF3 / OH /
alkoxy<(1-3)> / alkylthio<(1-3)> / alkylsulfinyl<(1-3)> /
alkylsulfonyl<(1-3)> / (SC Me)
G24 = Cl / alkyl<(1-3)> / alkoxy<(1-3)>
G25 = Hy<EC (1-3) Q (1-3) N (0) OTHERQ, AN (2-) C (0) N,
AR (0), BD (2) D, RC (1), RS (1) E6> (SO G24)
G27 = Hy<EC (1) Q (1) N (0) OTHERQ, AR (0), BD (ALL) SE,
RC (1), RS (1) M4 (1) X5> (SO G20)
G28 = Hy<EC (1-2) Q (1-2) N (0) OTHERQ, AR (0),
BD (ALL) SE, RC (1), RS (1) M6 (1) X7> (SO G20)
G29 = NULL / Ak<EC (-5) C, BD (0-) DE (0) T>
(SO (1-) G18) / (SC 398-5 399-7)

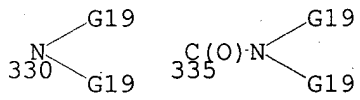


G30 = OH / 322 / (SC OMe)

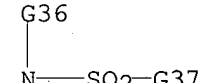


G31 = alkyl<(1-5)> / alkenyl<(3-5)> /
alkyl<(1-3)> (SR (1-) Ph) / cycloalkyl<(5-7)> /
alkyl<(1-3)> (SR cycloalkyl<(5-7)>) / 325

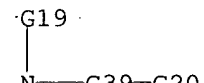
G32 = alkyl<(1-5)> / alkyl<(1-3)> (SR (1-) Ph) / Ph /
alkoxy<(1-3)> / 330 / **CO2H** / alkoxycarbonyl<(1-3)>
(SO (1-) Ph) / 335 / (SC Me / Et)



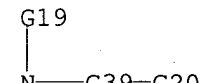
G33 = H / Me / Et / alkoxycarbonyl<(1-5)>
G34 = Me / OH / OMe / CN / CONH2 / H
G35 = (1) 394 / H



G36 = H / Me / Et
G37 = alkyl<(1-5)> / Ph / (SC Bu-n)
G38 = (1-) H / NH2 / 401 / OH



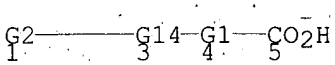
G39 = C(O) / SO2
G40 = (-1) 409 / H



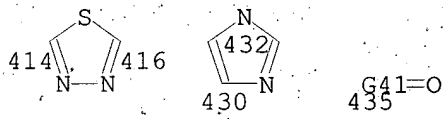
G41 = Hy<EC (1-) Q (0-) N (-2) S (-1) O (0) OTHERQ,
RC (1), RS (1) E5> (SO) / Hy<EC (1-) Q (0-) N (-2) S (-1)
O (0) OTHERQ, AR (1-), BD (6) N, RC (2),
RS (1) E5 (1) E6 (0) OTHER> (SO)
G42 = alkoxy<(1-3)> (SO (1-) aryl) /
alkylthio<(1-3)> (SO (1-) aryl) / NH2
DER: and tautomers and salts
MPL: claim 1
NTE: substitution is restricted

NTE: additional ring formation specified
NTE: also incorporates claim 10
STE: and stereoisomers

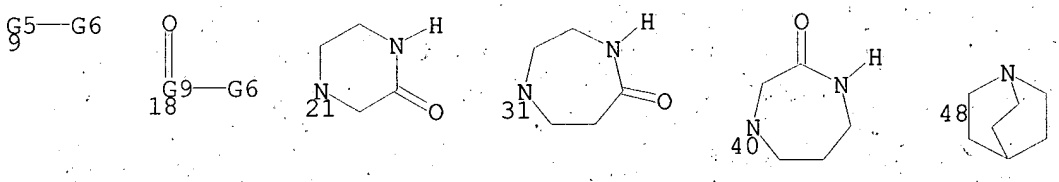
MSTR 2B

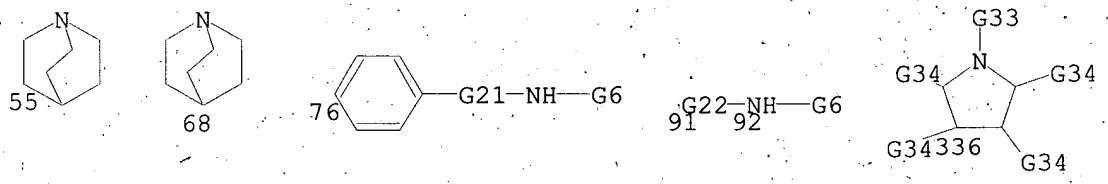


G1 = **Hy<EC (1-) Q (0-) N (-2) S (-1) O (0) OTHERQ, RC (1), RS (1) E5> (SO (1-3) G32)** / Hy<EC (1-) Q (0-) N (-2) S (-1) O (0) OTHERQ, AR (1-), BD (6) N, RC (2), RS (1) E5 (1) E6 (0) OTHER> (SO) / 435 / (SC 414-3 416-5 / 432-3 430-5)

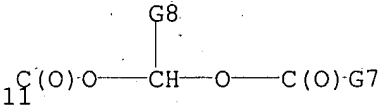


G2 = cycloalkyl<(5-7)> (SO (1-) G3) / 9 / 18 / 21 / 31 / 40 / pyridyl / 48 / 55 / 68 / 76 / 91 / (SC 336 / 346 / 363 / 375 / 387)

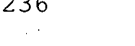




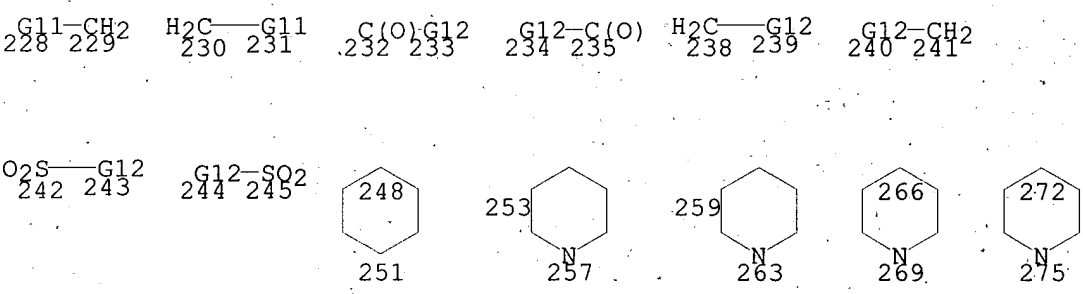
G3 = (-4) alkyl<(1-3)> / (-1) G4
G4 = OH / alkoxy<(1-3)> (SO Ph) / CN / CONH2 / **CO2H** / alkoxycarbonyl<(1-3)> (SO Ph)
G5 = **Hy<EC (4-6) C (1-2) Q (1-2) N (0) OTHERQ, AN (1-) C (1-) N, AR (0), BD (-1) DE (0) T> (SO (1-) G3)**
G6 = H / alkyl<(1-3)> / alkoxycarbonyl<(1-5)> / alkoxycarbonyl<(1-3)> (SR Ph) / alkenyloxycarbonyl<(3-5)> / cycloalkyloxycarbonyl<(5-7)> / 11



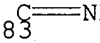
G7 = alkyl<(1-5)> / cycloalkyl<(5-7)> /
alkyl<(1-3)> (SR (1-) Ph) / alkoxy<(1-5)> /
cycloalkyloxy<(5-7)> / Ph
G8 = H / alkyl<(1-4)> / cycloalkyl<(5-7)> / Ph
G9 = Hy<EC (4-6) C (2) Q (2) N, AN (1-) C (2) N, AR (0),
BD (-1) DE (0) T> (SO (1-) G3)
G11 = O / S
G12 = NH / 236



G13 = alkyl<(1-3)> (SO (1-) Ph)
G14 = phenylene / Cb<EC (6) C, AN (2-) C, AR (1-),
BD (ALL) N, RC (1), RS (1) E6> (SO (1-2) G15) /
Hy<EC (1-2) Q (1-2) N (0) OTHERQ, AN (2-) C (0) N, AR (1-),
BD (ALL) N, RC (1), RS (1) E6> (SO G16) / 248-1 251-4 /
257-1 253-4 / 263-4 259-1 / 269-1 266-4 / 272-1 275-4 /
278-1 281-4 / alkylene / 228-1 229-4 / **230-1 231-4** /
232-1 233-4 / 234-1 235-4 / 238-1 239-4 / 240-1 241-4 /
242-1 243-4 / 244-1 245-4 / (SC 424-1 427-4 / CH2CH2)

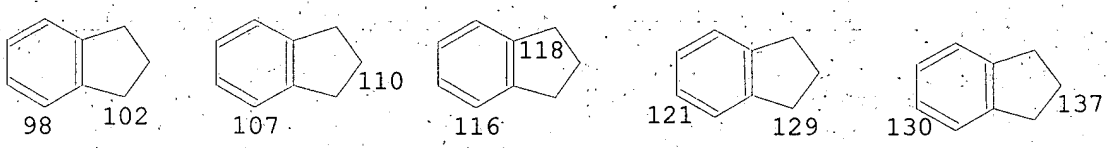


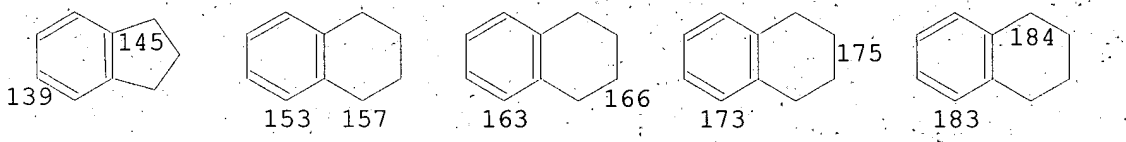
G15 = F / Cl / Br / alkyl<(1-3)> / CF3 / OH /
alkoxy<(1-3)> / alkylthio<(1-3)> / alkylsulfinyl<(1-3)> /
alkylsulfonyl<(1-3)> / (SC Me)
G16 = Cl / alkyl<(1-3)> / alkoxy<(1-3)>
G19 = H / alkyl<(1-3)> (SO (1-) Ph)
G21 = CH2 / 83

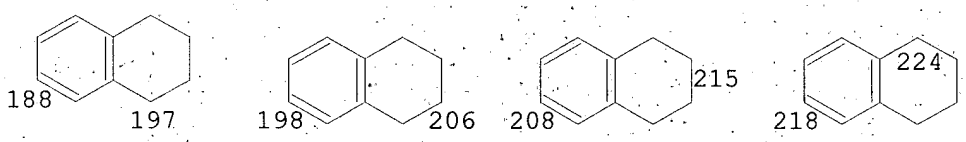


G22 = 102-92 98-3 / 110-92 107-3 / 118-92 116-3 /
129-92 121-3 / 137-92 130-3 / 145-92 139-3 / 157-92 153-3 /

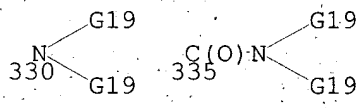
166-92 163-3 / 175-92 173-3 / 184-92 183-3 / 197-92 188-3 /
206-92 198-3 / 215-92 208-3 / 224-92 218-3







G32 = alkyl<(1-5)> / alkyl<(1-3)> (SR (1-) Ph) / Ph /
alkoxy<(1-3)> / 330 / CO2H / alkoxycarbonyl<(1-3)>
(SO (1-) Ph) / 335 / (SC Me / Et)

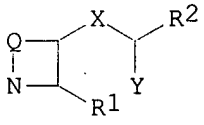


G33 = H / Me / Et / alkoxycarbonyl<(1-5)>
G34 = Me / OH / OMe / CN / CONH2 / H
G41 = Hy<EC (1-) Q (0-) N (-2) S (-1) O (0) OTHERQ,
RC (1), RS (1) E5> (SO) / Hy<EC (1-) Q (0-) N (-2) S (-1)
O (0) OTHERQ, AR (1-), BD (6) N, RC (2),
RS (1) E5 (1) E6 (0) OTHER> (SO)
DER: or reactive derivatives
MPL: claim 10
NTE: substitution is restricted
NTE: additional ring formation specified

L3 ANSWER 50 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 121:83070 MARPAT
TITLE: Azabicyclic tachykinin receptor antagonists
INVENTOR(S): Swain, Christopher John
PATENT ASSIGNEE(S): Merck Sharp and Dohme Ltd., UK
SOURCE: Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2268931	A1	19940126	GB 1992-15527	19920722
PRIORITY APPLN. INFO.:			GB 1992-15527	19920722

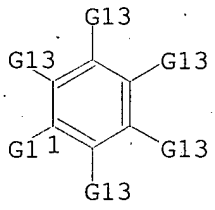
GI



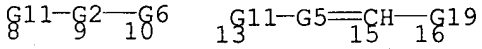
I

AB Title compds. [I; O = residue of an azabicyclic ring system; R1 = (halo)phenyl, trifluoromethylphenyl; R2 = (substituted)phenyl; X = O, S, CH2, etc.; Y = H, OH, halo, etc.] are claimed as tachykinin receptor antagonists (no data). No prepd. I are reported.

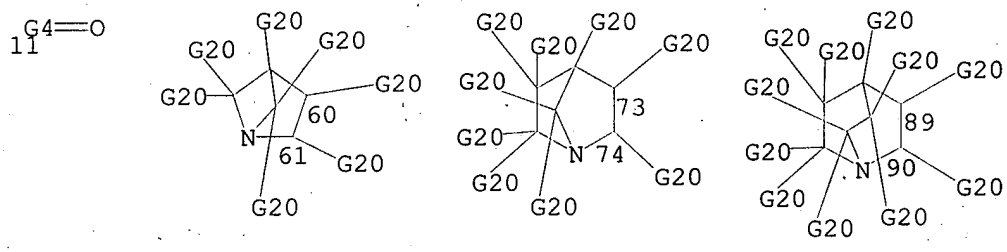
MSTR 1

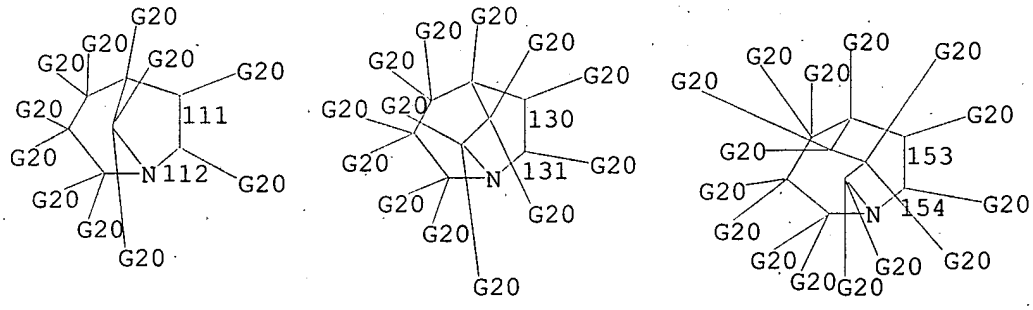


G1 = 10 / 16



G2 = **Hy<EC (2-) C (1) Q (1) N (0) OTHERQ, AN (2-) C, AR (0), RC (2)> (SO (1-) G3)** / 11 / (EX 60-10 61-8 / 73-10 74-8 / 89-10 90-8 / 111-10 112-8 / 130-10 131-8 / 153-10 154-8)



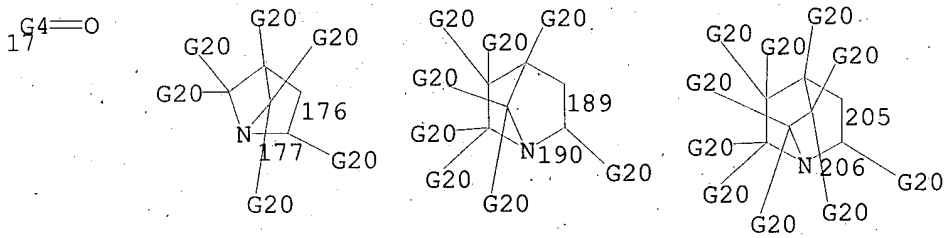


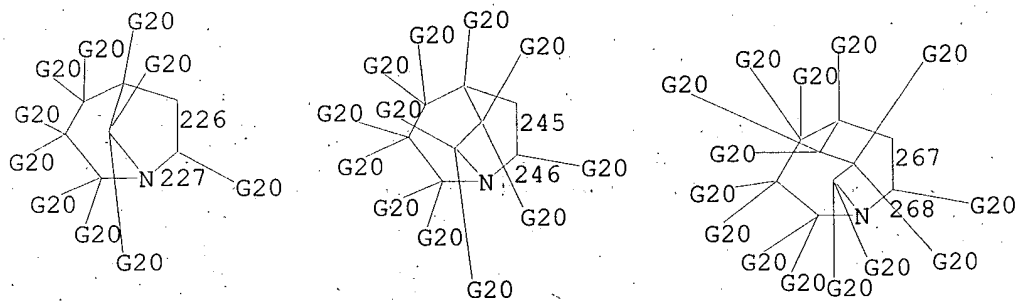
G3 = R / (EX alkyl<(1-4)> / alkenyl<(2-4)> /

alkynyl<(2-4)> / F / Cl / Br / I / OH / alkoxy<(1-4)> / **CO2H** / alkoxycarbonyl<(1-3)>)

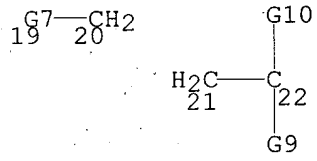
G4 = Hy<EC (3-) C (1) Q (1) N (0) OTHERQ, AN (3-) C, AR (0), RC (2)> (SO (1-) G3)

G5 = Hy<EC (2-) C (1) Q (1) N (0) OTHERQ, AN (2-) C, AR (0), RC (2)> (SO (1-) G3) / 17 / (EX 176-15 177-13 / 189-15 190-13 / 205-15 206-13 / 226-15 227-13 / 245-15 246-13 / 267-15 268-13)

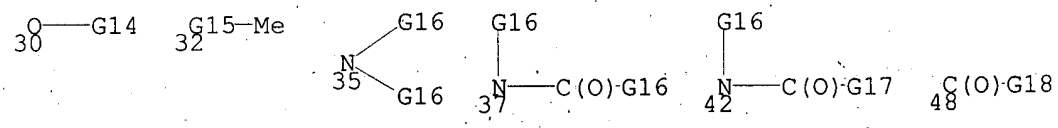




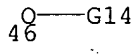
G6 = **20-1 19-9** / 22-1 21-9



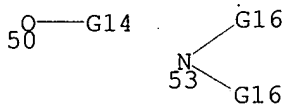
G7 = **O** / S
G8 = H / OH / F / Cl / Br / I
G9 = H / OH / F / Cl / Br / I
G10 = H
G11 = Ph (SO (1-) G12)
G12 = F / Cl / Br / I / CF3
G13 = (2-) H / alkyl<(1-6)> / alkenyl<(2-6)> / alkynyl<(2-6)> / F / Cl / Br / I / CN / NO2 / CF3 / SiMe3 / OH / 30 / 32 / 35 / 37 / 42 / **48**



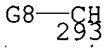
G14 = alkyl<(1-6)> / Ph / CF3
G15 = S / S(O) / SO2
G16 = H / alkyl<(1-6)> / Ph / CF3
G17 = OH / 46



G18 = **OH** / 50 / 53



G19 = 293 / C(O)

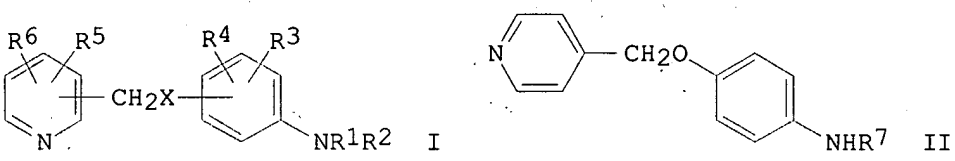


G20 = H / alkyl<(1-4)> / alkenyl<(2-4)> / alkynyl<(2-4)> / F / Cl / Br / I / OH / alkoxy<(1-4)> / CO2H / alkoxycarbonyl<(1-3)>
G9 +G10= O
DER: or salts or prodrugs
MPL: claim 1

L3 ANSWER 51 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 118:233895 MARPAT
TITLE: 2-quinolinyl methoxy compounds, medical uses and intermediates therefor
INVENTOR(S): Nielsen, Ole Bent T.; Ahfelt-Ronne, Ian
PATENT ASSIGNEE(S): Leo Pharmaceutical Products Ltd., Den.
SOURCE: U.S., 23 pp. Cont.-in-part of U.S. 5,109,009.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5157039	A	19921020	US 1990-633390	19901231
US 4826987	A	19890502	US 1986-834542	19860228
US 5109009	A	19920428	US 1990-581121	19900910
PRIORITY APPLN. INFO.:			GB 1985-6094	19850308
			GB 1985-25153	19851011
			US 1986-834542	19860228
			US 1987-140277	19871231
			US 1990-581121	19900910

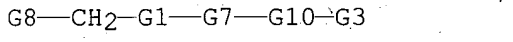
GI



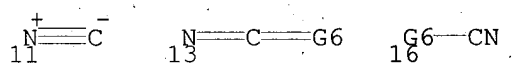
AB The title compds. [I; R1, R2 = H, (un)substituted alkyl, aryl, aralkyl; R3-R6 = H, halo, pseudohalo, cyano, NO2, amino, CO2H, OH, alkyl, alkoxy;

R5R6 = atoms required to form condensed, (un)substituted arom. ring; X = O, S, SO, SO2] were prepd. as arachidonic acid and histamine inhibitors, and drugs. Thus, 4-AcNHC6H4OH was condensed with 4-(chloromethyl)pyridine-HCl to give acetanilide II (R7 = Ac). This was deacetylated and methylated to give II (R7 = Me). At 10 .mu.M selected I gave 51-100% inhibition of antigen-induced histamine release from rat peritoneal mast cells.

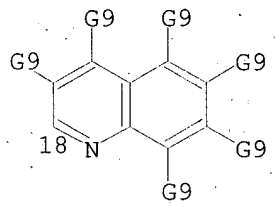
MSTR 2B

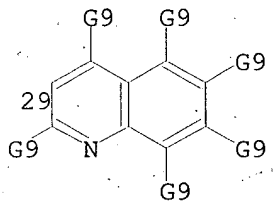


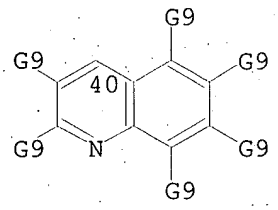
G1 = **O** / S / S(O) / SO2
G3 = Ak<(1-8)> (SO (1-) G4) / Ph (SO) / Cb<EC (6) C, AR (1-), BD (ALL) N, RC (1), RS (1) E6> (SO (1-) G4) / Ak<(1-4)> (SR (1-) G5)
G4 = X / N3 / CN / 11 / 13 / 16 / CF3 / NO2 / NH2 / CO2H / OH / alkyl / alkoxy

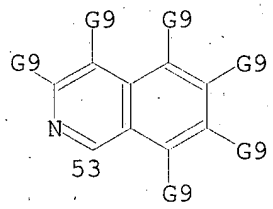


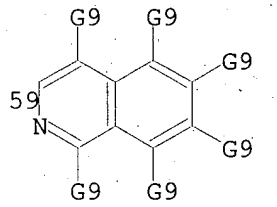
G5 = Ph (SO) / Cb<EC (6) C, AR (1-), BD (ALL) N, RC (1), RS (1) E6> (SO (1-) G4)
G6 = O / S / Se / Te
G7 = phenylene (SO) / **Cb<EC (6-10) C, AR (1-), BD (ALL) N, RC (1-2), RS (1-2) E6 (0) OTHER> (SO (1-2) G11)**
G8 = 4-pyridyl (SO (1-2) G11) / **Hy<EC (1-) Q (1-) N, AR (1-), BD (6-) N, RC (2), RS (1-) E6> (SO (1-2) G11)** / (EX 18 / 29 / 40 / 53 / 59 / 70)

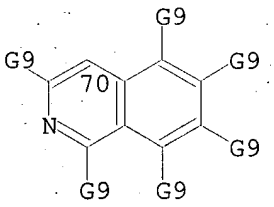




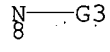




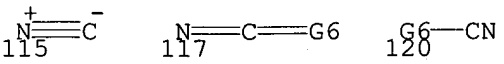




G9 = H / R
G10 = NH / 8



G11 = X / N3 / CN / 115 / 117 / 120 / NO2 / NH2 / **CO2H** / OH / alkyl / alkoxy



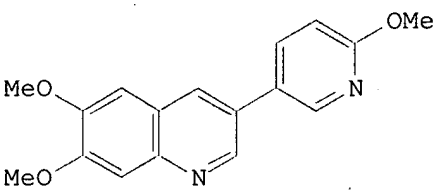
MPL: disclosure
NTE: substitution is restricted

L3 ANSWER 52 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 118:191764 MARPAT
TITLE: Bis mono- and bicyclic aryl and heteroaryl compounds (e.g., quinolines) which inhibit EGF and/or PDGF receptor tyrosine kinase
INVENTOR(S): Spada, Alfred P.; Maguire, Martin P.; Persons, Paul E.; Myers, Michael R.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer International (Holdings) Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9220642	A1	19921126	WO 1992-US3736	19920506
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
AU 9219934	A1	19921230	AU 1992-19934	19920506
AU 658646	B2	19950427		
EP 584222	A1	19940302	EP 1992-912051	19920506
EP 584222	B1	19971008		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06507643	T2	19940901	JP 1992-500068	19920506
AT 159009	E	19971015	AT 1992-912051	19920506
ES 2108120	T3	19971216	ES 1992-912051	19920506
US 5409930	A	19950425	US 1993-146072	19931108
US 5656643	A	19970812	US 1995-385258	19950208
CN 1187129	A	19980708	CN 1996-194512	19960606
US 36256	E	19990720	US 1997-988005	19971210
US 37650	E	20020409	US 2000-496399	20000202

PRIORITY APPLN. INFO.:
US 1991-698420 19910510
WO 1992-US3736 19920506
US 1992-988515 19921210
US 1993-146072 19931108
US 1993-166199 19931210
US 1994-229886 19940419
WO 1994-US14180 19941208
US 1996-652444 19960604

GI



I

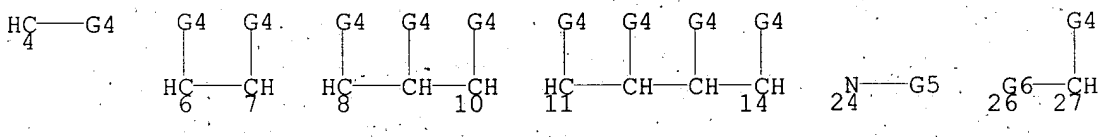
AB A method of using the title compds. in which a 1st ring system is (hetero)aryl, a 2nd ring system is (hetero)aryl or (hetero)carboxylic, and both ring systems are either (un)substituted monocyclic with 0-2 heteroatoms, or bicyclic with 0-4 heteroatoms, is claimed, along with pharmaceutical compns. and selected compds. Most of the prepd. and claimed compds. are quinolines and quinoxalines. The compds. are designed to inhibit abnormal cell proliferation, and their use for treating psoriasis, atherosclerosis, and vascular reocclusion is claimed. For example, coupling of 2-methoxy-5-(trimethylstannyl)pyridine with 6,7-dimethoxyquinolin-3-yl trifluoromethanesulfonate (prepns. given) in refluxing dioxane contg. Pd(PPh3)4 and LiCl gave pyridylquinoline deriv. I. The IC50 of I for inhibiting PDGF-R cell-free autophosphorylation was 0.030-0.070 .mu.M.

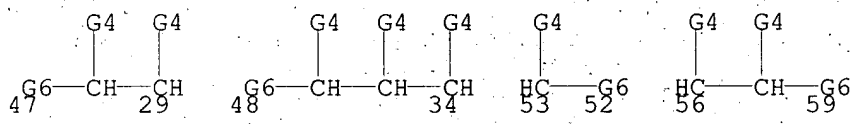
MSTR 1A

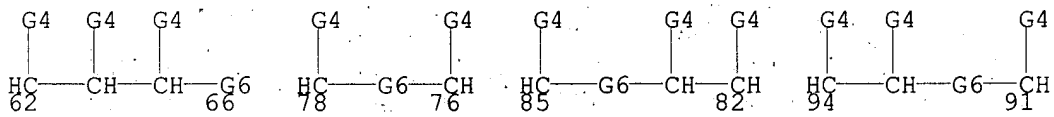
G1 = **Hy<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, AR (1-), RC (1-2), RS (0-) E5 (0-) E6 (0) OTHER> (SO (1-3) G7)**

G2 = Cb<RC (1-2)> (SO (1-3) G7) / **Hy<EC (1-) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1-2)> (SO (1-3) G7)**

G3 = 4 / 6-1 7-3 / 8-1 10-3 / 11-1 14-3 / O / NH / 24 / S / S(O) / SO2 / **26-1 27-3** / 47-1 29-3 / 48-1 34-3 / 53-1 52-3 / 56-1 59-3 / 62-1 66-3 / 78-1 76-3 / 85-1 82-3 / 94-1 91-3



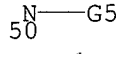




G4 = H / alkyl

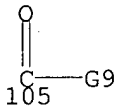
G5 = alkyl

G6 = **O** / NH / 50 / S / S(O) / SO2

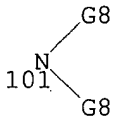


G7 = alkyl (SO (1-) aryl) / alkenyl (SO aryl) / Ph / OH / alkoxy (SO (1-) aryl) / acyloxy / X / alkyl (SR (1-) X) /

NH2 / alkylamino / dialkylamino / acylamino / **105** /
alkyl (SR alkoxycarbonyl) / alkenyl (SR alkoxycarbonyl)



G8 = cycloalkyl
G9 = **OH** / alkoxy (SO (1-) aryl) / NH2 / alkylamino /
dialkylamino / 101



DER: and pharmaceutically acceptable salts
MPL: claim 3

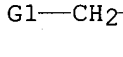
L3 ANSWER 53 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 115:130038 MARPAT
TITLE: Microbicidal deodorizing sprays containing silane compositions for domestic uses
INVENTOR(S): Mizuki, Fujio
PATENT ASSIGNEE(S): Dow Corning K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 03043483	A2	19910225	JP 1989-179641	19890712
JP 07068506	B4	19950726		

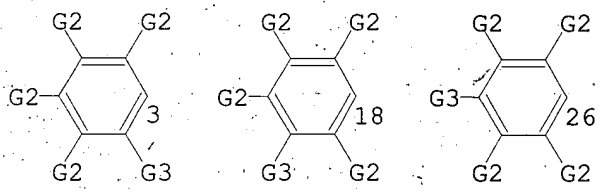
PRIORITY APPLN. INFO.: JP 1989-179641 19890712

AB An antimicrobial deodorant spray contains (1) silane derivs. R1R2R3N+R4S; X2X.Y- where X = alkoxy; Y = Br, Cl; R1, R2, R3 = C1-22 aliph. hydrocarbyl, one of which is C3-22 alkyl; R4 = C2-4 alkylene, CH2CH2CH2NHCH2CH2, (2) MeOH or EtOH, and (3) water. This compn. is stable for a prolonged period and does not produce gel during storage. A spray consisted of (MeO)3Si(CH2)3N+(CH3)2(C18H37)Cl-/MeOH mixt. (42:58% by wt.) 1.0, EtOH 70, and H2O 29% by wt. The spray may be used in bathroom and kitchen.

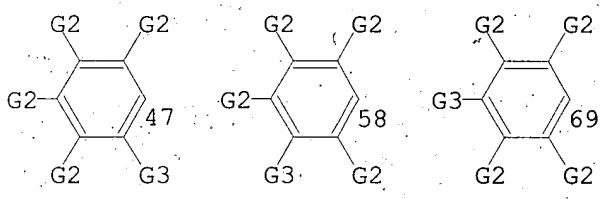
MSTR 1



G1 = 3 / **18** / 26



G2 = H / X
G3 = H / alkyl / NH2 / alkylamino / **CO2H** / alkoxycarbonyl / OH / alkoxy / NHCOMe
G4 = 47 / **58** / 69

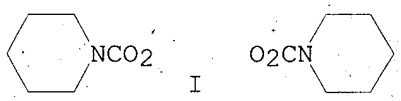


MPL: claim 1

L3 ANSWER 54 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 113:241606 MARPAT
TITLE: Urethane derivatives and liquid-crystal phases and display devices containing them
INVENTOR(S): Eidenschink, Rudolf; Prass, Ellen
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3837663	A1	19900510	DE 1988-3837663	19881105

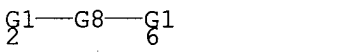
PRIORITY APPLN. INFO.: DE 1988-3837663 19881105
GI



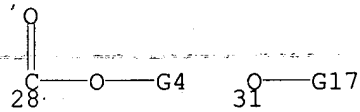
I II

AB The urethane derivs. have the general formula R1Q1(A1Z1)nA2Q2R2, where R1, R2 = C1-18 alkyl or alkenyl, optionally substituted with CN or .gtoreq.1 halogen, in which .gtoreq.1 CH2 group may be replaced by O, S, CO, OCO, COO, OCOO, or C.tplbond.C, R1 or R2 may be H, or 1 of the groups R1Q1 and Q2R2 may be F, Cl, CN, OCF3, or CF3; Q1,Q2 = COO, OCO, or a single bond; A1, A2 = (a) 1,4-phenylene in which 1 or 2 CH groups can be replaced by N, (b) 1,4-cyclohexylene in which 1 or 2 nonadjacent CH groups can be replaced by O or S, or (c) 1,4-cyclohexylene, 1,4-bicyclo[2.2.2]octylene, or piperidin-1,4-diyl, and (a) and (b) may be singly or multiply substituted with halogen, CN, and/or Me; Z1 = COO, OCO, CH2CH2, OCH2, CH2O, or a single bond; n = 1-3; .gtoreq.1 of the groups A1Z1 and A2Q2 = I; and/or .gtoreq.1 of the groups Q1A1 and Z1A2 = II.

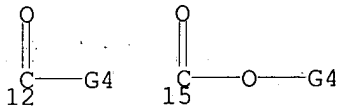
MSTR 1A



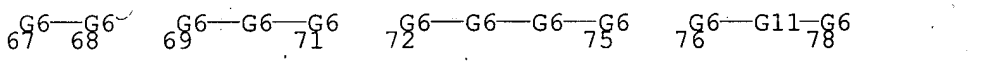
G1 = Ak (SO (1-) G2) / F / Cl / CN / OCF3 / CF3 / 28 / 31 / H / **CO2H** / OCHO / R

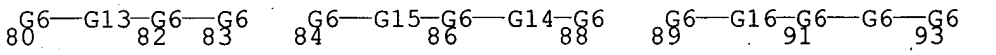


G2 = CN / R / 12 / 15



G4 = Ak (SO (1-) G5)
G5 = CN / X / R
G6 = **Cb<EC (6) C, RC (1), RS (1) E6 (0) OTHER> (SO)** / Hy<EC (1-2) Q (4-5) C (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) E6> (SO) / Cb<EC (8) C, BD (ALL) SE, FA (2) C, RC (2), RS (2) E6>
G8 = 67-2 68-6 / 69-2 71-6 / 72-2 75-6 / 76-2 78-6 / 80-2 83-6 / 84-2 88-6 / 89-2 93-6



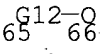


G11 = **65-76 66-78 / 66-76 65-78** / CH2CH2

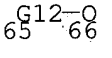
G12 = C(O) / **CH2**
G13 = **65-80 66-82 / 66-80 65-82** / CH2CH2

G14 = **65-86 66-88 / 66-86 65-88** / CH2CH2

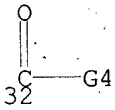
G15 = **65-84 66-86 / 66-84 65-86** / CH2CH2



G16 = **65-89 66-91** / **66-89 65-91** / CH2CH2



G17 = Ak (SO (1-) G5) / 32



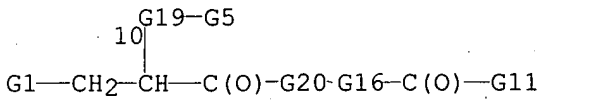
MPL: claim 1
NTE: substitution is restricted

L3 ANSWER 55 OF 55 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 112:234995 MARPAT
TITLE: Preparation of (mercaptoacylamino)arylcarboxylates as antihypertensives and enkephalinase inhibitors
INVENTOR(S): Doll, Ronald J.; Neustädt, Bernard R.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: U.S., 15 pp. Cont.-in-part of U.S. Ser. No. 250,035, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

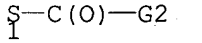
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4879309	A	19891107	US 1989-304881	19890130
WO 9003364	A1	19900405	WO 1989-US4068	19890925
W: AU, BB, BG, BR, DK, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 8943429	A1	19900418	AU 1989-43429	19890925
EP 364767	A1	19900425	EP 1989-117684	19890925
R: ES, GR				
US 4879309	B1	19920714	US 1991-90002263	19910130
PRIORITY APPLN. INFO.:			US 1988-250035	19880927
			US 1989-304881	19890130
			WO 1989-US4068	19890925

AB R1SCH2CH[(CH2)mR2]CONR4ACOR3 [I; A = pyridinediyl, (un)substituted phenylene; R1 = H, acyl; R2 = naphthyl, Ph2CH, (un)substituted Ph, PhO, PhCH2O, etc.; R3 = OH, (un)substituted NH2, alkoxy; R4 = H, alkyl, aralkyl; n = 0-3] were prepd. as antihypertensives and enkephalinase inhibitors (no data). Thus, BzSCH2CH(CH2Ph)COCl (prepn. given) was stirred 10 h with 3-H2NC6H4CO2H in pyridine to give BzSCH2CN(CH2Ph)CONHC6H4CO2H-3.

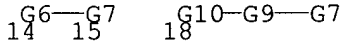
MSTR 1A



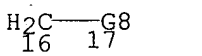
G1 = SH / 1



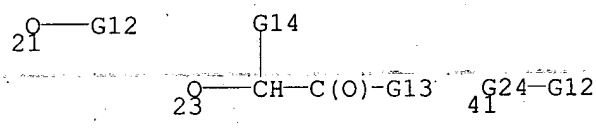
G2 = loweralkyl (SO (1-) G3) / alkoxy /
Cb<EC (6) C, AN (1-) C, AR (1-), BD (ALL) N, RC (1),
RS (1) E6> (SO (1-) G4) / Ph / Cb<EC (10) C, AR (1-),
BD (ALL) N, RC (2), RS (2) E6>
G3 = OH / loweralkoxy / loweralkylamino /
diloweralkylamino / Cb<EC (6) C, AR (1-), BD (ALL) N,
RC (1), RS (1) E6> (SO)
G4 = loweralkyl / cycloalkyl<(3-6)> / loweralkoxy / OH /
F / Cl / Br / I / CN / **CO2H** / loweralkoxycarbonyl / CH2NH2 /
CONH2 / aryl
G5 = Cb<EC (6) C, AN (1-) C, AR (1-), BD (ALL) N,
RC (1), RS (1) E6> (SO (1-) G4) / 14 /
Cb<EC (10) C, AN (1) C, AR (1-), BD (ALL) N, FA (2) C,
RC (2), RS (2) E6> / CHPh2 / 18 / Ph



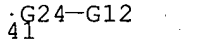
G6 = S / O / 16-15 17-10



G7 = **Cb<EC (6) C, AN (1-) C, AR (1-), BD (ALL) N,
RC (1), RS (1) E6> (SO (1-) G4)**
G8 = O / S
G9 = O / S / CH2
G10 = Cb<EC (6) C, AN (2-) C, AR (1-), BD (ALL) N,
RC (1), RS (1) E6> (SO (1-) G4)
G11 = **OH** / 21 / NH2 / 41 / 23



G12 = loweralkyl (SO (1-) G22)
G13 = NH2 / 41



G14 = H / alkyl (SO (1-) G15)
G15 = 28 / SH / alkylthio / NH2 / Ph /
Cb<EC (6) C, AR (1-), BD (ALL) N, RC (1), RS (1) E6>
(SR (1-) OH) / NHC(NH)NH2

C(O)—G25
28

G16 = Cb<EC (6-10) C, AN (2-) C, AR (1-), BD (ALL) N,
RC (1-2), RS (1-2) E6> (SO (1-) G4) /
Cb<EC (6) C, AN (2-) C, AR (1-), BD (ALL) N, RC (1),
RS (1) E6> (SR (1) 36) / phenylene /
(EX Hy<EC (1) Q (5) C (1) N (0) OTHERQ, AN (2) C, AR (1-),
BD (ALL) N, RC (1), RS (1) E6>)

G17—G18—G7
36

G17 = **O** / S
G18 = NULL / **CH2**
G19 = alkylene<(1-3)>
G20 = NH / 39

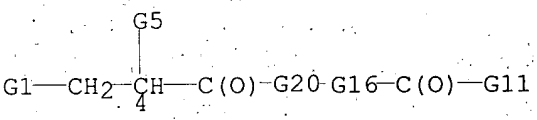
N——G21
39

G21 = loweralkyl (SO (1-) aryl)
G22 = OH / loweralkoxy (SO (1-) loweralkoxy) / X /
loweralkoxy (SR (1-) X) / NH2 / loweralkylamino /
diloweralkylamino / aryl (SO)
G24 = NH / 43

N——G12
43

G25 = OH / NH2
DER: or a pharmaceutically acceptable salt
MPL: claim 1

MSTR 1B



G1 = SH / 1

S—C(O)—G2
1

G2 = loweralkyl (SO (1-) G3) / alkoxy /
Cb<EC (6) C, AN (1-) C, AR (1-), BD (ALL) N, RC (1),
RS (1) E6> (SO (1-) G4) / Ph / Cb<EC (10) C, AR (1-),
BD (ALL) N, RC (2), RS (2) E6>
G3 = OH / loweralkoxy / loweralkylamino /
diloweralkylamino / Cb<EC (6) C, AR (1-), BD (ALL) N,
RC (1), RS (1) E6> (SO) / Ph
G4 = loweralkyl / cycloalkyl<(3-6)> / loweralkoxy / OH /
F / Cl / Br / I / CN / **CO2H** / loweralkoxycarbonyl / CH2NH2 /

CONH2 / aryl
G5 = Cb<EC (6) C, AN (1-) C, AR (1-), BD (ALL) N,
RC (1), RS (1) E6> (SO (1-) G4) / 14 /
Cb<EC (10) C, AN (1) C, AR (1-), BD (ALL) N, FA (2) C,
RC (2), RS (2) E6> / CHPh2 / 18 / Ph

G6—G7 G10—G9—G7
14 15 18

G6 = S / O / 16-15 17-4

H2C—G8
16 17

G7 = **Cb<EC (6) C, AN (1-) C, AR (1-), BD (ALL) N,**
RC (1), RS (1) E6> (SO (1-) G4)
G8 = O / S
G9 = O / S / CH2
G10 = Cb<EC (6) C, AN (2-) C, AR (1-), BD (ALL) N,
RC (1), RS (1) E6> (SO (1-) G4)
G11 = **OH** / 21 / NH2 / 41 / 23

O—G12 G14
21 |
O—CH—C(O)-G13 G24—G12
23 41

G12 = loweralkyl (SO (1-) G22)
G13 = NH2 / 41

G24—G12
41

G14 = H / alkyl (SO (1-) G15)
G15 = 28 / SH / alkylthio / NH2 / Ph /
Cb<EC (6) C, AR (1-), BD (ALL) N, RC (1), RS (1) E6>
(SR (1-) OH) / NHC(NH)NH2

C(O)—G25
28

G16 = Cb<EC (6-10) C, AN (2-) C, AR (1-), BD (ALL) N,
RC (1-2), RS (1-2) E6> (SO (1-) G4) /
Cb<EC (6) C, AN (2-) C, AR (1-), BD (ALL) N, RC (1),
RS (1) E6> (SR (1) 36) / phenylene /
(EX Hy<EC (1) Q (5) C (1) N (0) OTHERQ, AN (2) C, AR (1-),
BD (ALL) N, RC (1), RS (1) E6>)

G17—G18—G7
36

G17 = **O** / S
G18 = NULL / **CH2**
G20 = NH / 39

N---G21
39

G21 = loweralkyl (SO (1-) aryl)
G22 = OH / loweralkoxy (SO (1-) loweralkoxy) / X /
loweralkoxy (SR (1-) X) / NH2 / loweralkylamino /
diloweralkylamino / aryl (SO)
G24 = NH / 43

N---G12
43

G25 = OH / NH2
DER: or a pharmaceutically acceptable salt
MPL: claim 1

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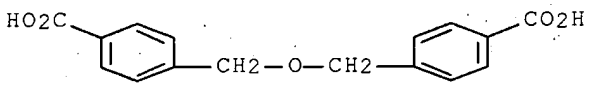
L12 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
AN 1989:593845 HCAPLUS
DN 111:193845
TI Kinetics and mechanism of the reaction of sodium hydroxide on 4-(halomethyl)-3-nitrobenzoic acids and the corresponding non-nitro derivatives in aqueous dioxane
AU Riad, Y.; El-Bardan, A.; Gundermann, K. D.
CS Fac. Sci., Alexandria Univ., Alexandria, Egypt
SO J. Chem. Res., Synop. (1989), (3), 78-9
CODEN: JRPSDC; ISSN: 0308-2342
DT Journal
LA English
OS CASREACT 111:193845
AB The relative rates for the hydrolysis [to give 3,4-R(HOCH2)C6H3CO2H (R = H, NO2)] and etherification [to give (2,4-R(HO2C)C6H3CH2)2O (R = H, NO2)] were detd. for 3,4-R(R1CH2)C6H3CO2H (R = H, NO2; R1 = halo) under the title conditions. The mechanism of the reactions are discussed. No ortho-effect is obsd.
IT **55255-64-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 55255-64-6 HCAPLUS
CN Benzoic acid, 4,4'-[oxybis(methylene)]bis- (9CI) (CA INDEX NAME)



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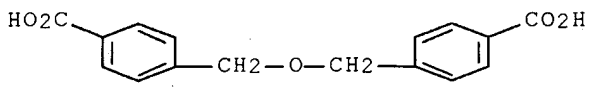
L12 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
AN 1987:176477 HCAPLUS
DN 106:176477
TI Reagents and synthetic methods. 57. Reduction of carbonyl compounds promoted by silicon hydrides under the influence of trimethylsilyl-based reagents
AU Aizpurua, Jesus M.; Lecea, Begona; Palomo, Claudio
CS Fac. Quim., Univ. Pais Vasco, San Sebastian, 20080, Spain
SO Can. J. Chem. (1986), 64(12), 2342-7
CODEN: CJCHAG; ISSN: 0008-4042
DT Journal
LA English
OS CASREACT 106:176477
AB 1,1,3,3-Tetramethyldisiloxane (I) in combination with iodotrimethylsilane or bromotrimethylsilane produces alkyl halides from aldehydes in good to excellent yields. Polymethylhydrosilane (II) in the presence of iodotrimethylsilane also produces benzyl iodides in excellent yields. On the contrary, II was unsuitable for the synthesis of benzyl bromides. Similarly, I in combination with trimethylsilyl triflate produces sym. ethers from aldehydes without concomitant formation of competitive products. Under similar conditions, II failed to provide the expected sym. ethers and Friedel-Crafts products were formed. Redn. of quinones to hydroquinones is also described.
IT **55255-64-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, by redn. of aldehyde by silicon hydride)
RN 55255-64-6 HCAPLUS
CN Benzoic acid, 4,4'-[oxybis(methylene)]bis- (9CI) (CA INDEX NAME)



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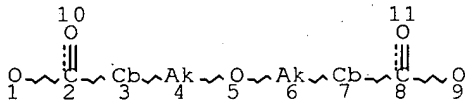
L4 700673 SEA FILE=REGISTRY ABB=ON PLU=ON L3 AND O>4
L7 STR



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CONNECT IS E2 RC AT 7
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DEFAULT MLEVEL IS ATOM
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GGCAT IS LIN LOC SAT AT 4
GGCAT IS LIN LOC SAT AT 6
GGCAT IS MCY UNS AT 7
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E6 C AT 3
ECOUNT IS E6 C AT 7

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L10 1 SEA FILE=REGISTRY SUB=L4 SSS FUL L7
L12 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L10